

# Variability in lipid profile among patients presented with acute myocardial infarction, unstable angina and stable angina pectoris

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**Abstract. – OBJECTIVE:** Despite the ample evidence and guidelines in treating coronary artery disease (CAD) with lipid-lowering therapy, physicians still have concerns in treating acute myocardial infarction (AMI) patients who have the low serum lipid level. We explored the adequacy of lipid-lowering therapy in treating AMI patients.

**PATIENTS AND METHODS:** Over 3000 CAD lipid profile data were collected, their data were divided into 3 groups (AMI; stable angina pectoris (SAP) and unstable angina pectoris (UAP) group) based their clinical characteristics. Statistical analyses were performed to compare their baseline lipid levels and clinical feature.

**RESULTS:** The total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c) and high-density lipoprotein cholesterol (HDL-c) level in AMI patients were the lowest, followed by UAP patient group and SAP patient group. There were significant differences in white blood count (WBC) and ejection fraction (EF) between 3 groups. A good correlation was confirmed between EF% and the lipid parameters of TC, LDL-c, HDL-c, non-HDL-c. WBC did not correlate with the lipid except HDL-c. AMI is an acute inflammatory reaction that is accompanied with the change of lipid level.

**CONCLUSIONS:** Although the level of TC, LDL-c and HDL-c are lower in AMI, but it is related with acute inflammatory reaction during the rupture of atherosclerotic plaques. Lipid-lowering therapy should not be delayed in treating AMI patients with lower lipid level.

*Key Words:*

Lipid, Coronary Artery disease, Inflammatory.

## Introduction

Aberrant serum total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-c) contribute significantly to the development of atherosclerosis<sup>1</sup>; they are also clinical manifestations of coronary artery disease. Numerous studies have

demonstrated that lipid-lowering therapy reduces the risk of first or recurrent cardiovascular events and improves survival in patients with coronary artery disease (CAD)<sup>2,3</sup>. Despite the convincing evidence and guidelines, lipid-lowering therapy has been less than optimal, especially in patients had acute myocardial infarction.

Fyfe et al<sup>4</sup> noted apparent decreases of TC in hospitalization of patients with an acute coronary syndrome (ACS) in 1971, later studies demonstrated that acute myocardial infarction (AMI) causes an acute-phase response, which includes increased cholesterol synthesis as well as concomitant increase in low-density lipoprotein cholesterol receptor activity, which results in reduction of LDL-c<sup>5-7</sup>. Pan et al<sup>8</sup> reported serial measurements result of 75 cases of AMI; they indicated a decline of all lipids level except lipoprotein (a) in plasma after patients were admitted to hospital. Mo<sup>9</sup> found high level of lipid in early stage of AMI. Wu et al<sup>10</sup> reported that serum level of LDL-c has no difference among acute myocardial infarction (AMI), unstable angina pectoris (UAP) and stable angina pectoris (SAP) patients. The differences of lipid levels were reported by studies derived from relative small population. Therefore, many physicians discount serum lipids obtained immediately upon admission for AMI, in part because of their understanding that such measurements are unreliable due to an early decrease in TC and LDL-c after AMI.

Recently, Wang et al<sup>11</sup> investigated 1242 AMI patients from 12 hospitals in Beijing, China, and they reported that lipid regulating agents were used only 43.6%. Accurate knowledge of baseline lipid levels may affect the selection of lipid-lowering therapy, and recognition of the potential need for adjunctive lipid therapy. This knowledge may also influence the patient's willingness to adhere to a recommendation for long-term lipid-lowering therapy.

Thus, to better understand the role of lipid regulating agent, it is necessary to collect additional observation data to shed light on the characteristics of presenting lipid levels of AMI patients. Here we report the retrospective analyses of a large data set of CAD collected from cardiology department in Tianjin Chest Hospital, China, to explore the relation between baseline lipid levels and clinical manifestations of coronary artery disease.

## Patients and Methods

This study was approved by an Institutional Review Board of Tianjin Chest Hospital, China (TXH-2007-06). The study was conducted in accordance with good clinical practice, all applicable regulatory requirements and the guiding principles of the Declaration of Helsinki. Written informed consent was obtained from all subjects prior to admission to the study.

Between November 2007 and July 2011, a total of 3245 patients admitted to cardiac department of our Hospital. Blood samples were obtained after patients were fasting on the first morning after admission. The serum lipid profile, blood routine, troponin I, creatine kinase, creatinine, liver function, were measured using standard hospital protocols. The blood routine, troponin I, creatine kinase and creatinine were performed immediately when the admitted patient was suspected as an AMI case. The demographic data of age, gender, cigarette smoking, hypertension (diagnose criteria<sup>12</sup>), diabetes mellitus (diagnose criteria<sup>13</sup>), and echocardiography were obtained from each patient.

According to their clinical characteristics, the patients were divided into 3 groups: AMI group included patients with acute myocardial infarction, who were diagnosed according to the criteria of Myocardial Infarction<sup>14</sup>. UAP group included patients who confirmed with a diagnosis of unstable angina pectoris according to Braundward's classification<sup>15</sup>, and angiographic evidence (documented stenosis > 50% by the American Heart Association classification in one or more principle coronary arteries). SAP group included patients with stable angina pectoris who was defined based on symptoms, specifically typical precordial chest pain from cardiac ischemia during exercise and from the findings of coronary angiography (documented severe stenosis of > 50% by the American Heart Association

classification in one or more principal coronary arteries).

Patients data were excluded if they were: (1) the onset of AMI was more than 24 hours; (2) lipid-lowering therapy for at least the preceding 3 months; (3) acute liver disease or hepatic dysfunction; (4) serum creatinine  $\geq$  2.0 mg/dl; (5) severe anemia; (6) systemic or pulmonary embolus; (7) acute infectious diseases and chronic inflammatory diseases; (8) hyperthyroidism and hypothyroidism.

## Statistical Analysis

Patients were divided into 3 groups of AMI, SAP and UAP. Wilcoxon rank sum tests were used for continuous variables and Chi-square tests for categorical variables. Data are presented as means  $\pm$  standard deviation (SD), or as percentage of baseline value. The differences of the lipid levels between the treatment groups were evaluated by Kruskal-Wallis Test. The relationships between the white blood count (WBC), ejection fraction (EF) and the lipid, lipoprotein variables were evaluated by linear correlation. *p* values < 0.05 were considered as statistically significant.

## Results

### Basic Data

The data from 3245 patients were included in the final analysis. The mean age of the population was  $60 \pm 10$ , and 63.8% were male. The clinical characteristics of the patients in the three groups were shown in Table I. There was no significant difference among the 3 groups regarding their age and alcohol consumption habits, while all other patient characteristics were significant difference ( $p \leq 0.01$ ).

### Demographic Data Comparison Results

For AMI patients, 36.5% of them have diabetes mellitus and 60.6% being smokers, which were higher than the other 2 groups. The serum levels of the lipids, lipoproteins, and apolipoproteins at admission are shown in Table II. We observed higher level of TC, TG, HDL-c, Apo A1, Apo B100, Non-HDL/HDL and LDL/HDL in SAP and UAP group as compared with AMI group ( $p \leq 0.05$ ). The differences were significantly ( $p \leq 0.01$ ) in TC, LDL-c, non-HDL-c, Apo A1, Apo B100, Non-HDL/HDL, TC/HDL and LDL/HDL in SAP group as compared with AMI group.

## Lipid profile among coronary artery disease

**Table I.** Demographic data of 3 groups' recruited patients.

	AMI (n = 876)	UAP (n = 1875)	SAP (n = 494)
Age (ys)	61 ± 11	61 ± 9	60 ± 9
Gender (M/F)	650/226 <sup>a</sup>	1137/738	286/208
Hypertension (%)	490 (55.9) <sup>a</sup>	1142 (60.9)	314 (63.6)
Diabetes mellitus (%)	320 (36.5) <sup>a</sup>	524 (27.9)	102 (20.6)
Drinking (%)	146 (16.7)	365 (19.5)	89 (18.0)
Smoking (%)	531 (60.6) <sup>a</sup>	967 (51.6)	261 (52.8)
Prior Stroke (%)	82 (9.4) <sup>a</sup>	241 (12.9)	36 (7.3)
Atorvastatin calcium user (40 mg)	458 (52.3%)	803 (42.8%)	256 (51.8%)
Fluvastatin user (80 mg QN)	418 (47.7%)	1072 (57.2%)	238 (48.2%)

<sup>a</sup>Significant difference among the 3 groups ( $p \leq 0.01$ ).

**Table II.** Comparison of different lipid levels between groups.

	AMI (n = 876)	UAP (n = 1875)	SAP (n = 494)
Total cholesterol (mg/dl)	183.1 ± 37.9	192.1 ± 44.4 <sup>a</sup>	213.8 ± 46.8 <sup>a,c</sup>
Triglycerides (mg/dl)	162.5 ± 113.3	168.3 ± 188.6 <sup>a</sup>	175.4 ± 116.8 <sup>a</sup>
LDL cholesterol (mg/dl)	116.6 ± 32.6	118.8 ± 39.4 <sup>a</sup>	139.1 ± 41.9 <sup>a,c</sup>
HDL cholesterol (mg/dl)	40.7 ± 10.8	45.4 ± 11.9 <sup>a</sup>	45.8 ± 13.2 <sup>a</sup>
Non-HDL cholesterol (mg/dl)	142.4 ± 34.4	146.7 ± 41.2	167.9 ± 45.2 <sup>a,c</sup>
Apolipoprotein A1 (mg/dl)	98.6 ± 17.1	108.9 ± 19.3 <sup>a</sup>	106.1 ± 20.7 <sup>a,c</sup>
Apolipoprotein B100 (mg/dl)	90.6 ± 20.7	97.6 ± 25.4 <sup>a</sup>	103.0 ± 25.2 <sup>a,c</sup>
Lpa (mg/dl)	30.7 ± 23.4	31.4 ± 25.4	31.2 ± 23.4
Non-HDL/HDL	3.7 ± 1.2	3.4 ± 1.3 <sup>a</sup>	3.9 ± 1.5 <sup>a,c</sup>
TC/HDL	4.9 ± 1.2	4.6 ± 1.2 <sup>a</sup>	5.2 ± 2.3 <sup>b,c</sup>
LDL/HDL	3.1 ± 1.0	2.9 ± 1.1 <sup>a</sup>	3.3 ± 1.2 <sup>a,c</sup>

<sup>a</sup>Significant difference among the 3 groups ( $p \leq 0.01$ ).

### Laboratory Measurement Results

As we can see from Table III, routine blood tests and EF comparison between groups revealed there were significant differences in WBC, neutrophils, lymphocytes and EF among 3 groups. Patients in AMI group had higher WBC and neutrophils level while SAP group had the lowest. There was significantly different EF between the 3 groups ( $p \leq 0.05$ ), while the

others measurements parameters (monocytes, hemoglobin, Platelet) were not significantly different.

### Correlation Analysis

We analyzed the correlation between WBC, EF and lipids parameters of TC, LDL-c, HDL-c, non-HDL-c, the results were listed in Table IV, as we can see, and a good correlation was con-

**Table III.** Different blood count and EF between groups.

	AMI (n = 876)	UAP (n = 1875)	SAP (n = 494)	p value
WBC ( $\times 10^9/L$ )	9.3 ± 2.9	7.0 ± 2.3	6.6 ± 1.5	0.000 <sup>a</sup>
Neutrophils (%)	71.5 ± 10.5	63.3 ± 9.0	61.8 ± 8.8	0.001 <sup>a</sup>
Lymphocytes (%)	19.9 ± 8.6	27.3 ± 8.3	28.7 ± 7.7	0.001 <sup>a</sup>
Monocytes (%)	7.0 ± 4.7	7.0 ± 4.8	6.8 ± 2.3	0.642
Hemoglobin (g/L)	136.6 ± 16.2	137.5 ± 15.2	138.8 ± 13.9	0.161
Platelet ( $\times 10^9/L$ )	213.2 ± 58.1	215.4 ± 53.8	216.8 ± 55.2	0.121
EF (%)	56.2 ± 9.2	62.0 ± 7.6	62.8 ± 8.0	0.001 <sup>a</sup>

<sup>a</sup>Significant difference among the 3 groups.

**Table IV.** Correlations (R) between lipid profile and WBC and EF.

	TC	LDL-c	HDL-c	non-HDL-c	Lipoprotein <sup>a</sup>
WBC	-0.030	0.004	-0.165 <sup>b</sup>	0.019	-0.019
EF (%)	0.081 <sup>b</sup>	0.037 <sup>a</sup>	0.096 <sup>b</sup>	0.057 <sup>b</sup>	-0.003

<sup>a</sup>Correlation significant at 0.05; <sup>b</sup>Correlation significant at 0.01.

firmed between EF and the lipids parameters, while WBC was not correlated with other lipids parameter except for HDL-c.

## Discussion

Fyfe et al<sup>4</sup> firstly reported the decreases in TC during hospitalization of patients with an ACS, later studies reported TC levels decreased in 2 days, the greatest decreasing occurs during days 4 to 12, and the levels ranged from 24% to 70% below baseline from different studies<sup>16-20</sup>, and remain stable after AMI when compared with a baseline level<sup>21,22</sup>. However, these earlier reports cannot lead to a clear conclusion or explain why ischemia may cause the changes of lipid profile. Our major finding in this study was that TC and LDL-c were the lowest in AMI group, followed by UAP and SAP group. UAP patient group had the intermediate level of TC and LDL-c; these findings imply that the level of TC and LDL-c were negatively related with stability of atherosclerotic plaque. Although no myocardial damage occurred in UAP patients, the level of TC and LDL-c in UAP were between the AMI and SAP.

Some early studies have shown that AMI cause an acute-phase response, which includes increased cholesterol synthesis as well as concomitant increase in LDL-c receptor activity, which results in reduction of LDL-c<sup>5,17,23,24</sup>. Myocardial necrosis produces an inflammatory process that results in migration of neutrophils into the injured region<sup>25,26</sup>. Our results also confirmed that the WBC and neutrophils in AMI group were highest in 3 groups, which imply that the inflammatory process generated in response to tissue injury.

The acute phase reactants measurement after AMI include C-reactive protein (CRP), serum amyloid A, fibrinogen etc. As positive reactants, CRP binds selectively with VLDL-c and LDL-c particles, possible interfering with the catabolism of VLDL<sup>27</sup>. Cytokine mediators were known to

account for the acute phase response after AMI *in vitro* studies suggested that cholesterol synthesis in HepGz cells was decreased by IL-1<sup>28</sup>, but increased by IL-6<sup>29</sup>. Thus, AMI is an acute inflammatory reaction accompanied by the change of lipid level. However, most of earlier studies reported the changes of TC and LDL-C during the restoration phase of AMI with little information on lipid level in these patients before the onset of disease due to the lack of the lipid check requirement.

Our data in the 3 groups of patients implied the conformation courses of the atherosclerotic plaques. The declining trend of TC and LDL-C from SAP patient group to UAP and to AMI group promotes the conclusion that the changes of lipid level are accompanied by the rupture of atherosclerotic plaques. This conclusion is supported by the past research which showing the inflammatory reaction occurred during the restoration of AMI. We deduct that the inflammatory reaction are closely related with the changes of lipid level during the course of AMI, which is the course of the rupture of atherosclerotic plaques. The cause-effect relationship between inflammatory reaction and changes in lipid level still needs future investigation; this could offer new insights into the theoretical basis for treatments of CAD. In the present study of ACS patients receiving statin therapy, the addition of high-sensitivity C-reactive protein (hs-CRP) to lipid-based treatment could significantly improve their risk prediction. Measuring CRP during treatment may therefore offer additive prognostic information to lipids in ACS patients<sup>30</sup>. Lipid lowering agents have well known anti-inflammatory action<sup>31</sup>, it is particularly important in the treatment of CAD. Lipid lowering agent should be used throughout the course of atherosclerosis regardless the lipid level of CAD.

We recommend administering lipid lowering agent to AMI patients immediately at their admission to hospital without concern of the lower level of TC and LDL-c. The lower level of TC and LDL-c are likely the results of acute inflam-

matory during the formation of AMI, which may persist. It is critically important that the lipid lowering agent be used to treat AMI without contraindication, as recommended by the American Heart Association (AHA)/American College of Cardiology (ACC)<sup>31</sup>. The observation of the decreased of TC and LDL-c in UAP patient without lipid-lowering therapy may suggest the instability of atherosclerotic plaques, which may be aggravated into AMI. It is important to pay close attention to these UAP patients and enhance lipid-lowering therapy in order to prevent AMI.

Studies suggested that non-optimal high-density lipoprotein cholesterol levels are highly prevalent in patients presenting with acute coronary syndromes<sup>32</sup>. Our study demonstrates that HDL-c was the lowest in AMI patients, and the highest in SAP patients, this supports the previous conclusion.

### Conclusions

Although the level of TC, LDL-c and HDL-c are lower in AMI, and it is related to acute inflammatory reaction during the rupture of atherosclerotic plaques, lipid-lowering therapy should not be delay with the lower lipid profile in AMI patients.

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### Conflict of Interest

The Authors declare that there are no conflicts of interest.

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