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PROGNOSTIC VALUE OF HIGH-SENSITIVITY C-REACTIVE PROTEIN AND LIPOPROTEIN (a) IN ACUTE MYOCARDIAL INFARCTION PATIENTS RECEIVING EMERGENCY PERCUTANEOUS CORONARY INTERVENTION

PROGNOSTIČKA VREDNOST VISOKOOSETLJIVOG C-REAKTIVNOG PROTEINA I LIPOPROTEINA (a) KOD PACIJENATA SA AKUTNIM INFARKTOM MIOKARDA PODVRGNUTIH HITNOJ PERKUTANOJ KORONARNOJ INTERVENCIJI

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Summary: In order to study the prognostic value of high-sensitivity C-reactive protein (hsCRP) and lipoprotein (a) [Lp(a)] in patients receiving emergency percutaneous coronary intervention (PCI) following acute myocardial infarction (AMI), we retrospectively reviewed 118 patients who received emergency PCI following AMI from January 2007 to April 2010. The plasma levels of hsCRP and Lp(a) were determined. The incidence of cardiovascular events was compared between patients with an elevated hsCRP level and those with a normal hsCRP level and between patients with an elevated Lp(a) level and those with a normal Lp(a) level. Results showed that the incidence of cardiovascular events was 52.9% in the hsCRP-elevated group and 18.2% in the hsCRP-normal group displaying a significant difference (P=0.011). However, the incidence of cardiovascular events was 35.3% in the Lp(a)-elevated group and 46.4% in the Lp(a)-normal group and statistical analysis revealed no significant difference (P=0.733). HsCRP, but not Lp(a), can serve as a prognostic factor for patients receiving emergency PCI following AMI.

Keywords: high-sensitivity C-reactive protein, lipoprotein (a), acute myocardial infarction, emergency percutaneous coronary intervention, prognosis

Kratak sadržaj: Kako bi se utvrdila prognostička vrednost visokoosetljivog C-reaktivnog proteina (hsCRP) i lipoproteina (a) [Lp(a)] kod pacijenata podvrgnutih hitnoj perkutanoj koronarnoj intervenciji (PKI) posle akutnog infarkta miokarda (AIM), retrospektivno je analizirano 118 pacijenata podvrgnutih hitnoj PKI posle AIM između januara 2007. i aprila 2010. Određeni su nivoi hsCRP i Lp(a) u plazmi. Upoređena je incidenca kardiovaskularnih događaja kod pacijenata sa povišenim nivoom hsCRP i onih sa normalnim nivoom hsCRP, kao i između pacijenata sa povišenim nivoom Lp(a) i onih sa normalnim nivoom Lp(a). Rezultati su pokazali da je incidenca kardiovaskularnih događaja bila 52,9% u grupi sa povišenim hsCRP i 18,2% u grupi sa normalnim hsCRP, što je ukazalo na značajnu razliku (P=0,011). Međutim, incidenca kardiovaskularnih događaja bila je 35,3% u grupi sa povišenim Lp(a) i 46,4% u grupi sa normalnim Lp(a), a statistička analiza nije otkrila značajnu razliku (P=0,733). HsCRP, ali ne i Lp(a), može poslužiti kao prognostički faktor kod pacijenata podvrgnutih hitnoj PKI posle AIM.

Ključne reči: visokoosetljivi C-reaktivni protein, lipoprotein (a), akutni infarkt miokarda, hitna perkutana koronarna intervencija, prognoza

Introduction

Acute myocardial infarction (AMI) is the most severe type of coronary heart disease (CHD) and threatens the human health. Emergency primary percutaneous coronary intervention (PCI) has been a treatment of choice for myocardial infarction patients

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with ST segment elevation or high risk. Primary PCI can reduce the mortality and the complications of AMI and improve the prognosis in these patients (1, 2). However, there is still a fraction of patients who develop several complications including cardiogenic shock, heart failure and severe arrhythmia following emergency primary PCI, which finally results in death or decrease in quality of life. Thus, screening these patients is helpful to take timely measures to reduce the mortality and the complications of AMI. High sensitivity C-reactive protein (hsCRP) and lipoprotein (a) [Lp(a)] have been demonstrated to be independent risk factors for cardiovascular events in patients with CHD (3, 4). In the present study, we reviewed the AMI patients with ST segment elevation or high risk in our hospital from January 2007 to April 2010. The levels of hsCRP and Lp(a) were measured and the prognostic value of both parameters was evaluated in these patients.

Patients and Methods

Patients

A total of 118 AMI patients receiving emergency PCI in our hospital were recruited from January 2007 to April 2010 and divided into 4 groups according to the hsCRP level and Lp(a) level. The clinical information of these patients is shown in *Table I*. There were no marked differences in the ages, gender, types of myocardial infarction, pre-operative Killip grade of cardiac function and time to PCI among the groups. Before emergency PCI, 300 mg of aspirin and 600 mg of Plavix were orally administered to patients, who were then intravenously injected with tirofiban hydrochloride at a dose of 10 mg/kg within 3 min and then at a dose of 0.15 mg/kg/min for maintenance. During the PCI, heparin was administered at a dose of 60–80 U/kg and the dose of heparin was adjusted according to the ACT. Percutaneous transluminal coronary angioplasty (PTCA) was performed in all patients followed by stenting with rapamycin-eluting stents. After surgery, aspirin (300 mg once daily and then 100 mg once daily 3 months later) and Plavix (75 mg once daily for at least 1 year) were orally administered and the patients were intravenously injected with tirofiban hydrochloride at 36 h. Four hours after surgery, the femoral artery catheter was removed and the patients were subcutaneously treated with low molecular weight heparin (100 AXaIU/kg) once every 12 h for 2–8 days. Other drugs included nitrates, angiotensin-converting enzyme inhibitors (ACEI), beta-blocker and diuretics which were administered according to disease condition. Patients with acute or chronic infection, systemic immune diseases, malignancies, recent history of surgery or abnormal liver function were excluded.

Diagnostic criteria

The diagnosis of AMI was based on the typical ischemic chest pain, electrocardiogram (ECG) and myocardial enzyme levels. Indications for emergency

Table I Clinical information of patients in different groups

Group	N	Male: female	Age (yr)	Infarct area (N)					
				non-ST-segment elevation	extensive anterior	inferior	high lateral	extensive anterior + inferior	inferior + lateral
Lp(a) elevation group	34	26:8	61.2±12.8	3	15	7	3	3	3
Lp(a) normal group	84	74:10	62.7±10.7	3	34	28	7	3	9
Group	Killip grade of cardiac function (N)				Serum lipid (mmol×L^{-1})				Time from admission to PCI (min)
	I	II	III	IV	TC	LDL-C	HDL-C	TG	
Lp(a) elevation group	15	9	5	5	4.25±1.62	2.15±0.78	1.22±0.54	1.09±0.32	84.3±18.9
Lp(a) normal group	44	19	6	15	5.01±1.88	2.82±1.12	1.16±0.62	1.25±0.38	86.5±17.9

Table II Incidence of cardiovascular events in patients with elevated and normal hsCRP

hsCRP	N (patients)	$\bar{x} \pm$ SD (mg/L)	Heart failure	Shock	Severe arrhythmia	Death	N (events)	Incidence (%)
elevation	85	10.10±4.37	11	23	3	8	45	52.9%*
normal	33	1.64±0.59	3	3	0	0	6	18.2%

*P<0.05 (χ^2 = 13.109, p = 0.011)

Table III Incidence of cardiovascular events in patients with elevated and normal Lp(a)

Lp(a)	N (patients)	$\bar{x} \pm$SD (mg/L)	Heart failure	Shock	Severe arrhythmia	Death	N (events)	Incidence (%)
elevation	34	499.8±174.5	3	7	1	1	12	35.3%$^{\Delta}$
normal	84	164.5±65.9	11	19	2	7	39	46.4%

P>0.05 (χ^2 = 2.014, p = 0.733)

PCI were determined and the PCI was done within 12 h after admission. PTCA and stenting with rapamycin-eluting stents were carried out in all patients.

Detections

On the second day following admission, the fast venous blood (4 mL) was obtained and the serum collected by centrifugation. The hsCRP level was measured with a transmission immunoturbidimetric assay and hsCRP ≥3 mg/L was defined as elevation of the hsCRP level. Lp(a) was measured with an immunoturbidimetric assay and Lp(a) ≥300 mg/L was defined as elevation of Lp(a).

Reagents and instruments

An automatic biochemical analyzer (7170A, Hitachi), hsCRP detection kits (Finland, Orion Diagnostica Oy) and Lp(a) detection kits (Sekisui Medical Technology [Japan] Ltd) were used in the present study.

Statistical analysis

Statistical analysis was performed with SPSS version 11.5 and comparisons between the two groups were done with the chi square test. A value of $P < 0.05$ was considered statistically significant.

Results

The incidence of heart failure, cardiogenic shock, severe arrhythmia (ventricular fibrillation, ventricular flutter, sustained ventricular tachycardia, third-degree atrioventricular block, type 2 second-degree atrioventricular block and supraventricular tachycardia with hemodynamic changes) and death in the patients with hsCRP elevation and those with normal hsCRP is shown in *Table II*. Statistical analysis showed a significant difference between the patients with elevated and normal hsCRP. The incidence of cardiovascular events in the patients with Lp(a) elevation was comparable to those in the patients with normal Lp(a) (*Table III*).

Discussion

Atherosclerosis is a chronic inflammation per se and the occurrence and development of CHD are closely related to the inflammation. When the myocardial infarction is present, the damage and necrosis of the myocardium can recruit and activate the mononuclear macrophages and subsequently lead to massive release of tumor necrosis factor (TNF) and interleukin-6 (IL-6) which can induce the synthesis of acute phase proteins including CRP in the hepatocytes. CRP is a non-specific marker of inflammation and is closely associated with atherosclerosis. Studies have confirmed that CRP is an independent risk factor for CHD and can be applied as a risk factor to predict cardiovascular diseases (5, 6). A special technique with high sensitivity can be used to measure the CRP at a low level (<10 mg/L) and this type of CRP is also known as hsCRP. As compared to traditional CRP detection, the hsCRP assay has the advantages of high sensitivity, high accuracy and favorable repeatability. Increasing attention has been paid to the application of hsCRP assay in the diagnosis of cardiovascular diseases (7). Ortolani et al. (8) evaluated the predictive value of high sensitivity (hs) C-reactive protein levels on long-term survival in patients with ST-elevation myocardial infarction (STEMI) treated

with primary PCI, and they found the patients with hs-C-reactive protein > or = 3.1 mg/L showed lower estimated survival, lower estimated myocardial infarction-free survival and lower estimated event-free survival. By multivariable analysis hs-C-reactive protein appeared to be an independent predictor of long-term mortality, long-term mortality and re-infarction and adverse events. The serum Lp(a) level is related to the genetics and is not affected by gender, age, body weight, physical exercise and cholesterol-lowering drugs. The distribution of Lp(a) in the healthy population is abnormal and 300 mg/L is usually defined as a threshold value. Patients with Lp(a) of >300 mg/L have high risk for CHD (4). To date, no studies have been conducted to investigate the prognostic value of hsCRP and Lp(a) in patients receiving emergency PCI.

Our study showed AMI patients undergoing emergency PCI with an elevated hsCRP level had a higher incidence of cardiovascular events including shock, heart failure, severe arrhythmia and death when compared with those with a normal hsCRP level, which suggests hsCRP has prognostic value in these patients. This may be attributed to the fact that hsCRP reflects the degree of inflammation in the body. However, prognostic value of Lp(a) was not noted in these patients. Based on the present study, we speculate that hsCRP measurement should be performed in every patient receiving emergency PCI, which would be helpful in determining the disease condition and prognosis. In addition, it is necessary to develop measures to lower the hsCRP level (such as application of statins) aiming to improve the prognosis of patients receiving emergency PCI and guide the pharmacotherapy during the peri-PCI period.

Conflict of interest statement

The authors stated that there are no conflicts of interest regarding the publication of this article.

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