The research on screening function of myeloperoxidase in chest pain patients compared with coronary CT angiography

MA Chun-mei[1], *GUO Yue-ling[1], WU Jian-rong, YE Dao-bin, DENG Xiao-wei, LIU Hui-liang

Health Care Center, the Hospital of Chinese People's Armed Police Forces, Beijing 100143; GUO Yue-ling, co-author with equal contribution of the first author, Department of Medical Engineering, Beijing Military General Hospital, Beijing 100125, China

Abstract: Objective: To explore the value of myeloperoxidase in screening patients with chest pain in early time. Methods 324 individuals were recruited and divided into coronary heart disease (CHD) group (165 cases) and non-coronary heart disease group (NCHD) (159 cases) according to the result of coronary CT angiography (CTA). CHD patients were divided into two groups, acute coronary syndrome (ACS) group and stable angina pectoris (SAP) group. We collected plasma samples in each group, and myeloperoxidase (MPO) levels were detected in plasma. MPO concentrations were detected by enzyme-linked immunosorbent assay (ELISA). Gensini scores were used to assess coronary artery lesions. **Results** The plasma MPO levels were significantly higher in CHD group than those in NCHD group ($p<0.01$). Patients with ACS had significantly higher MPO concentrations than those with SAP. MPO in the CHD patients had close relations with Gensini score. Sensitivity, specificity and total consistent rate of MPO were 79.39%, 96.22%, and 87.65% respectively. Kappa value (0.75, $P<0.05$) showed that the MPO level was in good agreement with CTA. **Conclusions:** The plasma MPO level can help us identify patients with chest pain in early time. MPO level has clear relations with the width of coronary artery.

[MA Chun-mei, GUO Yue-ling, WU Jian-rong, YE Dao-bin, DENG Xiao-wei, LIU Hui-liang. **The research on screening function of myeloperoxidase in chest pain patients compared with coronary CT angiography.** *Life Sci J* 2014;11(12):1050-1053]. (ISSN:1097-8135). http://www.lifesciencesite.com. 180

Key words: myeloperoxidase; chest pain; coronary artery disease; coronary CT angiography(CTA)

Chest pain is a common reason that patients go to internal medicine department, and most chest pain is result from coronary heart disease (CHD). As the most common cardiovascular disease (CVD), CHD can lead to many other medical complications and has high case fatality. Therefore, it is of great significance in early stage if CHD can be identified among numerous patient with chest pain and the degree of coronary artery disease can be predicted. Study has proved that myeloperoxidase (MPO) plays a great role in promoting atherosclerotic formation, development, plaque instability and even rupture, and also the formation of thrombogenesis[1]. Foreign research shows, MPO level can indicate the risk of CVD independently, without relying on C-Reactive Protein (CRP) or other inflammation markers[2]. Testing the MPO level of chest pain patients can suggest the risk of adverse cardiac events in the future[3]. This study aims at discussing the value of plasma MPO level in identifying CHD of chest pain patients and correlations MPO level has with the width of coronary artery.

1 Subjects and Methods

1.1 Research Objects

The research objects are patients who have chest pain and went to the Health Care Center and the Outpatient Department of Cardiology of the Hospital of Chinese People's Armed Police Forces, from April 2012 to April 2014. All patients were divided into two groups after coronary CT angiography: (1) Coronary heart disease (CHD) group: 165 cases, composed of 121 males and 44 females, and the mean age is 63.59±12.68 yrs. Among which exists 78 cases of stable angina pectoris (SAP), with 56 males and 22 females, the average age is 61.55±12.52 yrs; while there exists 87 cases of acute coronary syndrome (ACS), with 65 males and 22 females, the mean age is 62.39±11.80 yrs. The selection of ACS and SAP patients referred to the ACC/AHA guidebook. (2) Non-coronary heart disease (NCHD) group: 159 cases, composed of 109 males and 50 females, and the mean age is 61.18±9.88 yrs. All patients received examinations such as electrocardiography, chest X-ray, and blood biochemistry test, and have no diseases such as peripheral vascular diseases, surrounding blood thrombotic diseases, autoimmune disease, malignancy, severe trauma, acute and chronic infectious diseases, severe liver and kidney inefficiency.

1.2 Methods

1.2.1 Sample Collection and Dispose

2-3ml venous blood was collected, and put it in a heparin lithium anticoagulant tube. The collected sample was centrifuged at the speed of 3000r/min for 10 min, and then plasma was obtained. The separated plasma usually can maintained for no longer than 8h at room temperature (20-26℃).

1.2.2 Test Methods

Quantitative detection kit (enzyme-linked immuno sorbent assay, ELISA) produced by Beijing Xiehe Unionluck Biotechnology Co. was used to detect plasma MPO concentrations. The detecting instrument used was the SUNRISE microplate reader from Tecan Trading Co., an Austrian company.

1.2.3 Coronary Artery CTA Examination

Coronary angiography was examined by 64-MSCT (SOMATOM Definition AS128, Germany). CTA images were analyzed through Syngo circulation software. The patients rested for 20-30min in peace before taking coronary artery examination, so as to keep their heart rate below 70 bpm. With no contraindication, patients whose heart rate exceeds 70 bpm took beta-blocker (Betaloc or Propranolol) and 2mg Estazolam to keep their heart rates at about 65 bpm. The patients first hold their breath during the CT scan, and then received chest plain CT scan. Nonionic contrast media (Ultravist) was injected into a vein in the front of the patients' elbows by high pressure injector to enhance the scan. All the data would be transferred to Vitrea 2 imaging software after scanning for postprocessing and three-dimensional reconstruction.

1.2.4 Coronary Aniogram and Evaluation of Degree of Coronary Artery Stenosis

The coronary vessels image segmentation evaluation standards set by the American Heart Association and Gensini scores were used to assess the degree of coronary artery stenosis of each vessel: score 1, stenosis rate <25%; score 2, stenosis rate ⩾ 25%-50%; score 4, stenosis rate⩾50%-75%; score 8, stenosis rate⩾75%-90%; score 16, stenosis rate⩾ 90%-99%; score 32, stenosis rate ⩾ 90%-99%. Coronary artery stenosis scores multiplied by corresponding coefficient showed different results, for example, left main coronary artery (LMCA) lesion: score × 5; left anterior descending branch (LADB) lesion: proximal segments of coronary artery score× 2.5, middle segments of coronary artery score×1.5; diagonal branch (DIAG) lesion: first diagonal branch score×1, second diagonal branch×0.5; left circumflex (LCX) artery lesion: proximal segments of coronary artery score×2.5, far segments of coronary artery score×1, posterior descending branch×1, posterior side branch × 0.5; right coronary artery disease: proximal, middle and far segments of coronary artery score×1. For each patient, the total score of each lesion branch equals to the score of his/her coronary artery disease stenosis degree.

1.3 Statistical Analysis

The SPSS 19.0 software was adopted for statistical analysis. Measurement data was described through geometric mean ± standard deviation ($\overline{X}$ ± S), and t-test was chose to compare two groups of data, when P<0.05 there exists statistical significance. F-test was used to analyze measurement data, X2 –test for enumeration data. Kappa test (P<0.05) was employed to check the consistency of the results of this methods and coronary artery CT. And if the Kappa statistics> 0.7, then it indicates that they are in good agreement with each other.

2.Results

2.1 Common Clinical Situation Comparison

In terms of age and the ratio of patients with combined hyperlipidemia, there's no significant difference between the CHD group and NCHD group (P>0.05); CHD group has higher ratio of combined hypertension and diabetes mellitus patients than NCHD group, and the difference is statistically significant (P<0.05); CHD patients apparently have higher MPO level than NCHD group, and the difference is statistically significant (P<0.01). See Table 1.

Table 1. Comparisons between CHD Group and NCHD Group

Items	CHD GROUP (n=165)	NCHD GROUP (n=159)	X^2/F	*P*
Gender(Male/Female)	121/44	109/50	0.90	0.34
Age(y)	62.39±11.80	61.18±9.88	1.43	0.23
Case No. of Hypertension(%)	113(68.48%)	25(15.72%)**	92.19	0.00
Case No. of Diabetes(%)	64(38.78%)	42(26.42%)*	5.63	0.02
Case No. of Hyperlipemia(%)	114(69.09%)	119(74.84%)	1.33	0.25
Smoker No.(%)	56(35.22%)	41(24.84%)	2.57	0.11
MPO(ng/ml)	109.77±41.63	39.82±18.87**	19.36	0.00

Notes: Comparing with CHD group, $^{*}P<0.05$, $^{**}P<0.01$.

2.2 MPO Detection Results

The MPO diagnose cut-off value is 94.01ng/ml, when MPO≥94.01ng/ml, which is positive, the laboratory diagnosis is CHD; while MPO<94.01ng/ml, which is negative, the laboratory diagnosis is NCHD. Among 165 CHD cases under coronary artery CT tests, 131 cases have positive MPO results, and 34 cases have negative MPO results. Among 159 NCHD cases, 6 cases have positive MPO results, and 153 cases have negative MPO results. Sensitivity, specificity and total consistent rate of MPO were 79.39%, 96.22%, and 87.65% respectively. Kappa test ($P < 0.05$) was employed to check the consistency of the results of this methods and coronary artery CT. And the Kappa value is 0.75, which indicates that they are in good agreement with each other.

2.3 Comparison of MPO Concentrations among Subgroups of CHD Group

The CHD group is divided to ACS group and SAP group. ACS group apparently have higher MPO concentrations (120.95±68.55ng/ml) than SAP group (85.19±32.69ng/ml), and the difference is statistically significant ($t=4.20$, $P<0.01$).

Based on Gensini score, quantitative analysis was adopted to analyze the vascular disease degree of CHD group (165 patients) and they were divided to: scores≤4, scores between 5-10, scores between 11-39, and scores ≥ 40. The MPO concentration rose as the Gensini scores went up, and difference existed in each subgroup ($F=4.14$, $P<0.05$, see Table 2).

Table 2 MPO Level Comparison between Different Coronary Artery Group ($\overline{X}$ ±S)

Group Type	Subgroup Gensini score	Case No.	MPO Concentration(ng/ml)
CHD		165	109.77±41.63*
	≤4	46	95.74±48.40
	5-10	71	109.29±35.65
	11-39	25	114.65±38.29
	≥40	23	130.08±35.70

3. Discussion

Many studies have confirmed that myeloperoxidase (MPO) plays an important role in the occurrence and development of coronary heart disease (CHD), in terms of endothelial cell injury, lipidosis, intima dysplasia, plaque formation, and rupture. On the one side, MPO has oxidation effect on low density lipoprotein and high density lipoprotein[4-5]; on the other side, MPO can damage the endothelial cells[6]. It can cause cerebral vasospasm, bring plaque erosion and rupture[7], therefore, MPO has a positive effect on atherosclerosis. Studies have shown that MPO, as a new independent risk factor of coronary heart disease (CHD), can predicate the occurrence, development and outcome of CHD[8].

This research result shows that the sensitivity, specificity and total consistency rate of MPO were 79.39%, 96.22%, and 87.65% respectively. Kappa value (0.75, $P<0.05$) showed that the MPO level was in good agreement with CTA, which also has statistical significance. Therefore, MPO concentration can be applied in the screening of coronary heart disease (CHD) of patients with chest pain. And this results are similar to that of Ma Qinghua's[9-10].

In addition, study found that the CHD group apparently have higher MPO level than NCHD group, so did the plasma MPO level. ACS group apparently have higher plasma MPO concentrations than SAP group ($p<0.01$). Moreover, 165 patients with CHD were divided into different groups with Gensini scores according to their vasculopathy degrees. MPO concentrations were clearly related to Gensini scores of the degree of coronary artery lesions. The higher Gensini scores, the higher MPO concentrations, which showed the correlation between MPO level and the degree of coronary artery lesions. Thus, detecting plasma MPO levels can help to diagnose the severity of coronary artery lesions of coronary heart disease (CHD) patients.

In conclusion, detecting plasma MPO levels can help to identify patients with chest pain in early time. MPO, as a kind of new inflammation marker, its expression and rising competent indicates the occurrence and development of coronary heart disease (CHD). As a result, MPO has an important clinical significance on rapid, accurate prediction on whether the patients with cheat pain will get CHD. Inspecting plasma MPO concentration is a new experimental method to identify CHD and diagnose the severity of coronary artery lesions in early time. It can greatly help to screen susceptible population, and to reduce coronary artery and to improve prognosis. It is particularly suitable for the early screening of outpatients with cheat pain, such as in physical examination, outpatient clinic, or preliminary screening of suspected coronary heart disease (CHD) in basic medical institution.

References

1. Shiu SW, Xiao SM, Wong Y, et al. Carbamylation of LDL and its relationship with myeloperoxidase in type 2 diabetes mellitus. Clinical Science, 2014, 126:175-181.
2. Cayley WE Jr. Prognostic value of myeloperoxidase in patients with chest pain. N Engl J Med, 2004, 350:516-518.
3. Searle J, Shih J, Muller R, et al. The role of

myeloperoxidase (MPO) for prognostic evaluation in sensitive cardiac troponin I negative chest pain patients in the emergency department. Eur Heart J Acute Cardiovasc Care, 2013, 2: 203-210.
4. Meuwese MC, Stroes ES, Hazen SL, et al. Serum myeloperoxidase levels are associated with the future risk of coronary artery disease in apparently healthy. J Am Coll Cardiol, 2007, 50:159-165.
5. Bergt C, Pennathur S, Fu X, et al. The myeloperoxidase product hypochlorous acid oxidizes HDL in the human artery wall and impairs ABCA1-dependent cholesterol transport. Proc Natl Acad Sci USA, 2004, 101:13032-13037.
6. Stocker R , Huang A, Jeranian E, et al. Hypochlorousacid impairs endothelium-derived nitric oxide bioactivity through a superoxide-dependent mechanism. Arterioscler Thromb Vasc Biol, 2004, 24:2028-2033.
7. Landmesser U, Hornig B, Drexler H. Endothelial function: a critical determinant in atherosclerosis? Circu-lation, 2004, 109: II27-33.
8. Shiu SW, Xiao SM, Wong Y, et al. Carbamylation of LDL and its relationship with myeloperoxidase in type 2 diabetes mellitus. Clin Sci, 2014, 126:175-181.
9. 马庆华，邓爱云，张钲，等．髓过氧化物酶对胸痛患者的临床意义．检验医学，2013，28:25-29.
10. Brennan ML, Penn MS, Van Lente F, et al. Prognostic value of myeloperoxidase in patients with chest Pain. N Engl J Med, 2003, 349:1595 - 1604.

12/19/2014