REVIEW

Appraisal of the Prognosis in Patients with Acute Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention*

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ABSTRACT Acute myocardial infarction (AMI) is still the leading factor causing crippling and death in cardiovascular disease. Percutaneous coronary intervention (PCI) can significantly reduce inpatient mortality and incidence of complication. But owing to the existence of restenosis, in-stent thrombosis, etc., recurrent post-PCI cardiovascular events and high repeatability of hospitalization, as well as its crippling rate and mortality, remain a serious threat to the society and the patients' family. Therefore, the appraisal and intervention in post-PCI associated risk factors has presently become one of the foci in clinical research. To improve the near- and long-term prognosis and quality of life in post-PCI AMI patients, further improvement of the evaluation system in risk factors and prognosis is necessary in order to provide a theoretical basis for early application of intervention in high-risk patients in clinical practice. This thesis mainly dissertates some explicit and valuable factors for clinical prognosis evaluation in recent studies, involving C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), brain natriuretic peptide (BNP), atrial natriuretic peptide (ANP), Chinese medicine (TCM) syndrome, their correlation with clinical state and course of AMI, and their importance in clinical prognosis.

KEY WORDS myocardial infarction, percutaneous coronary intervention, prognosis

Percutaneous coronary intervention (PCI) is a landmark advance in the therapeutic history of acute myocardial infarction (AMI), which could reduce inpatient mortality and incidence of complications. But the existence of restenosis, in-stent thrombosis and so on increases the risk for recurrence of cardiovascular events in post-PCI patients(1). Along with the development of drug eluting stents (with drugs for anti-inflammation, anti-transportation, anti-proliferation, pre-treatment, etc.), the nuisance of restenosis was somewhat alleviated, and its immediate effect has been affirmed by some randomized controlled trials. But the long-term effectiveness and safety of the revolutionary technique remains a vexing problem(2). Therefore, the evaluation and intervention in the post-PCI associated risk factor is one of the foci in clinical studies that attracted much attention from all over the world in the recent years. Some explicit factors valuable for clinical prognosis and affirmed by current research, include C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), brain natriuretic peptide (BNP) and atrial natriuretic peptide (ANP) as well as Chinese medicine (CM) syndromes with regarding to their correlation with the condition and course of AMI patients. These are discussed in this thesis, and their values for clinical prognosis evaluated.

C-reactive Protein
CRP is a kind of protein discovered by Pearson, et al(3) which is synthesized and secreted by hepatocytes and is capable of binding with cell wall C-amylose of pneumococci. As a nonspecific inflammation marker, its concentration in blood is positively proportionate with the degree of tissue damage. In case that other inflammatory factors have been excluded, the level of CRP could present the intensity of inflammatory reaction in coronary lesions. Hypersensitive CRP (hs-CRP) is a new independent forecasting index for coronary heart disease (CHD), with the strongest forecasting effect of all the 12 markers for cardiovascular diseases.

Research by Li, et al(4) shows that in ST-segment elevation AMI patients after emergent PCI, left ventricular ejection fraction (LVEF) was lower and peak values of WBC count and creatine kinase isozyme were higher in patients with raised hs-CRP than in those with normal hs-CRP. One hundred and eighty days after PCI, the incidence of cardiac adverse events in the former was significantly higher than in the latter. Multiple factor analysis displayed that the hs-CRP level determined on the very day of hospitalization is the main independent factor for forecasting adverse cardiac events in ST-

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segment elevation AMI patients 180 days after emergent PCI. But the research conducted by Gach, et al(8) shows that post-PCI transient elevation of hs-CRP could forecast the main malignant cardiac events more strongly than the pre-PCI or post-PCI high hs-CRP level.

Anzai, et al(6) indicated that in patients who experienced one Q-wave AMI, the peak value of CRP is a key factor for forecasting short- and long-term prognosis. The peak was rather lower in non-senile patients, presenting angina before myocardial infarction or with successful recanalization, while irregular elevation of CRP level was often revealed in patients with heart rupture. The possibility of heart rupture, ventricular aneurysm and cardiogenic death within one year would be greatly increased in case of CRP>20 mg/dL. A study by Smit, et al(7) illustrated that in patients with ST-elevated PCI, the pre-PCI high CRP level shows obvious correlation with re-infarction rate and mortality within one year after PCI.

Some research displayed that CRP level is raised after AMI and the degree of which is related with the infarcted area to a certain extent(8,9). PCI could result in temporal elevation of CRP levels, which might be related with the stimulation of stent on plaque, endothelial injury, plaque rupture and aggravation of local inflammatory reaction. From this it could be seen that since the degree of inflammation, which could be represented by CRP level, is an important cause for post-PCI restenosis, CRP level should definitely be of value in forecasting the occurrence of restenosis.

**Tumor Necrosis Factor-α**

TNF-α is a kind of pre-inflammatory cytokine mainly produced by activated mononuclear macrophage, as well as an important and negatively regulatory factor for growth. It could promote the adhesion between endothelial cells and white blood cells, stimulate endothelial cells to secrete inflammatory mediators, activate the blood coagulation system, suppress fibrinolysis, increase inflammatory exudation and oxygen free radical production, and accelerate the release of interleukin-1, -6 and -8 by mononuclear macrophage, etc. so as to promote the occurrence and development of inflammation(10,11). TNF-α is the key factor in triggering and promoting "cascade amplification" induced excessive inflammatory reaction, and thus, plays an important role in the pathophysiologic development process of myocardial ischemia/reperfusion injury(12). Studies in recent years show TNF-α could be secreted also by mature cardiac muscle cells and vascular endothelium is one of its important targets(13,14). Therefore, TNF-α induced vascular endothelial injury is of vital meaning in the pathogenesis of many cardiovascular diseases.

It has been shown by Li, et al(15) that the serum level of TNF-α is escalated along with the exacerbation of myocardial ischemia, i.e. that in AMI patients pectoris > in patients with unstable angina > in patients with stable angina pectoris > in normal persons. Thus, it can be regarded as a fine index for myocardial ischemia.

Animal experiments have proven that the myocardial infarct area, vascular endothelial injury, endothelin release and lipid peroxidation injury of cells in patients could be reduced significantly by effectively neutralizing plasma TNF-α with its own mon- antibody(16). It was also proven by Kubica, et al(17) that the inflammatory activation degree in the peri-operative stage could influence the long-term prognosis of post-PCI patients. The level of TNF-α is significantly related with the re-infarction rate and incidence of adverse cardiovascular events in patients.

Another report(18) shows that in the course of AMI, the evident rise of plasma TNF-α with earlier peaking is a clue for severe conditions and bad prognosis in the near future. It has been found that the patients’ peripheral plasma level of TNF-α that was determined 4-8 weeks after they were discharged from hospital (hospitalized for CHD events, including post-AMI angina pectoris, re-infarction, heart failure and even sudden death) was significantly higher than in those without CHD events, suggesting that the persistent post-AMI high level of TNF-α expression might be of definite significance in predicting post-AMI recurrence of CHD events.

Observation by Théroux, et al(19) found that the mortality and incidence of cardiac shock in elevated ST-segment AMI patients after PCI would be high if they presented high TNF-α level post-PCI. High levels of inflammatory reaction in 72 h after PCI were evidently correlated with the mortality of patients within 90 days. However, for post-PCI prognosis evaluation, the value of TNF-α level is inferior to that of CRP level.

Many studies illustrated that in AMI patients, the level of TNF-α is correlated with the course and severity of the illness to a definite extent, as it could evidently rise after PCI, which could be taken as an index for post-PCI adverse event forecasting. This is of great significance in evaluating short- and long-term prognosis of AMI patients. It has been displayed in a study(20) that the gene type of TNF-α could be regarded as a risk forecasting factor for occurrence of restenosis in post-PCI patients and suppressing the secretion of TNF-α may be a new way of thinking for restenosis prevention in clinical practice.