Inflammation plays an important role not only in the initiation and progression of atherosclerosis but also in plaque rupture of coronary artery disease (CAD) [1–3], which leads to acute coronary syndrome (ACS) or even acute myocardial infarction (AMI). It is well known that C-reactive protein (CRP) is one of the most important inflammation markers and has been proved to be an independent risk factor for CAD [4–7]. High level of CRP predicts poor clinical outcomes in patients with both stable CAD and ACS [6–9]. Compared with CRP, high-sensitivity CRP (hs-CRP) is more sensitive that can be examined in serum. However, the source of CRP or hs-CRP in CAD or ACS has not been definitively explored.

One hypothesis suggested that elevated hs-CRP, which can be measured in systemic circulation, is released from unstable or ruptured plaque in coronary circulation, and then transported to systemic circulation [10]. Another hypothesis suggested that elevated hs-CRP is released from non-coronary circulation tissue (liver cells and fatty tissues) and then transported to coronary circulation, which transforms stable plaque into an unstable or ruptured one, and finally induces ACS or AMI [11,12]. Whether hs-CRP originates from systemic or coronary circulation is still a controversial issue [10–12]. Besides, monocyte is an important chronic inflammatory factor and secretes cytokines such as interleukin-1, interleukin-6, and tumor necrosis factor-α, which stimulates the production of CRP [1–4]. Large amount of monocytes may induce high level of hs-CRP, which predicates high risk of ACS or AMI for patients with CAD.

Here, we compared the level of hs-CRP between systemic and coronary circulation in patients with AMI and stable CAD, as well as the difference of monocyte between patients with AMI and stable CAD. The study included 80 patients (60 patients with AMI and 20 patients with single-vessel stable CAD) hospitalized in the Department of Cardiology, the First Afflicted Hospital of Nanjing Medical University from July 2012 to April 2013. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000 [5]. Informed consent was obtained from all the included patients.

In the AMI group, coronary angiography was immediately performed after admission, and the time window from the onset of chest pain to the balloon dilatation ranged from 2 to 12 h. In the stable CAD group, patients received coronary angiography 1–2 days after admission. Blood sample was collected from both systemic and coronary circulation. Blood sample of systemic circulation was taken from peripheral arterial puncture, while intracoronary blood sample was taken by using a ‘Diver’ catheter over the wire to the distal site of plaque in the culprit vessel.

Fasting blood sample from each site was collected in the coagulation-promoting tubes, and centrifuged at 2100 g for 10 min. Serum was separated and immediately analyzed. Serum level of hs-CRP (mg/l) was measured by the method of rate nephelometry, using Siemens BN-II Special Protein Analyzer (Bonn, Germany). Meanwhile, the level of monocytes (10⁹/l) from systemic circulation was measured.

To explore the source of hs-CRP, the difference of hs-CRP level between systemic and coronary circulation was evaluated in each patient. Paired Student’s t-test revealed that the level of hs-CRP was higher in blood sample from systemic circulation than that from coronary circulation in the AMI group (mean difference (MD): 0.67, n = 60, 95% confidence interval (CI): 0.08–1.26, P = 0.0266); there was no significant difference between systemic and coronary circulation in the stable CAD group (MD: 0.18, n = 20, 95% CI: −0.03 to 0.39, P = 0.09) (Fig. 1). There was a trend towards higher MD of hs-CRP between systemic and coronary circulation in the AMI group than that in the stable CAD.
Comparing the level of monocyte from systemic circulation between the AMI group and the stable CAD group, the AMI group showed a higher level of monocytes than that in the stable CAD group (0.47 vs. 0.36; MD: 0.11, 95% CI: 0.001–0.22, \( P = 0.05 \)). Logistic regression analysis showed that a high level of monocyte might be a risk factor for AMI \( (P = 0.053) \).

These data showed that hs-CRP from systemic circulation was higher than coronary circulation in the AMI group, while there was no significant difference between systemic and coronary circulation in the stable CAD group, and the level of monocyte was higher in the AMI group than that in the stable CAD group.

In summary, our results demonstrated that hs-CRP originates from systemic circulation rather than coronary circulation. The elevated hs-CRP was probably released from non-coronary circulation tissue due to stimulation of chronic inflammation and transported to coronary circulation, which transformed stable plaque into an unstable or ruptured one, and finally induced ACS or AMI. Meanwhile, monocyte, a chronic inflammatory factor, might be associated with the production of hs-CRP and participate in this process.

Given that hs-CRP predicts poor clinical outcomes for patients with CAD [5–9] and is increased in the process of chronic inflammations, such as periodontitis, bronchitis, and arthritis [1–4], reducing inflammation reaction may decrease the risk of plaque rupture and provide a protective effect to AMI. Therefore, anti-inflammatory drugs such as statins, aspirin, and angiotensin-converting enzyme inhibitor or angiotensin receptor blocker should be prescribed to the patients with CAD in the early period.

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