Increased inflammatory response in patients with the first myocardial infarction and nonsignificant stenosis of infarct-related artery

Pojачан инфламаторни одговор код болнога са првим инфарктом миокарда и несигнifikантном стеноzem инфарктне артерије

Nenad Ratković*†, Dragan Đinčić*†, Branko Gliđić*†, Snježana Vukotić*, Aleksandra Jovelić‡, Slobodan Obradović*†

*Clinic for Emergency and Internal Medicine, Belgrade, Serbia; †University of Defence, Faculty of Medicine of the Military Medical Academy, Belgrade, Serbia; ‡Institute for Cardiovascular Diseases, Sremska Kamenica, Serbia

Abstract

Introduction/Aim. Atherosclerosis presents a serial of highly specific cellular and molecular responses, and could be described as inflammatory diseases. Accordingly, for development of acute myocardial infarction (AMI), structure and vulnerability of atherosclerotic plaque are more important than the extent of stenosis of infarct-related artery. Consequently, inflammation and atherosclerosis and its complications are in good correlation. C-reactive protein (CRP) as nonspecific inflammatory marker, has prognostic significance in coronary artery diseases. The aim of this study was to establish the correlation between inflammatory response expressed as levels of CRP and fibrinogen in serum and extent of coronary artery stenosis. Methods. Study included 35 patients with acute myocardial infarction, as the first manifestation of coronary artery disease, which were treated with thrombolytic therapy according to the guidelines. All the patient had a reperfusion. The patients with acute or chronic inflammatory diseases, an increased value of sedimentation, fibrinogen, CK

Apstrakt

Uvod/Cilj. Ateroskleroz predstavlja seriju visokospecifičnih celularnih i molekularnih odgovora, koji se najbolje mogu opisati kao inflamatorno oboljenje. U tom kontekstu, za nastanak akutnog infarkta miokarda (AIM) sastav i vulnerability aterosklerotske plombe mogu biti značajniji od stepena stenoze infarktne arterije (IA), odnosno biološko, inflamatorno stanje može biti pokazatelj kojim će se brzinom i sme- rom razvijati ateroskleroz i njene kompleksije. Glil rada bio je da se ustanovi da li postoji korelacija između inflamatornog odgovora, prikazanog c-reaktivnim proteinom (CRP) i fibri- nogenom i stepena stenoze infartne arterije (IA) kod bolesnika sa AIM, kao prvom manifestacijom koronarne bolesti.

Metode. Istraživanjem je bilo obuhvaćeno 35 bolesnika sa AIM, kao prvom manifestacijom koronarne bolesti, koji su lečeni tromboličkom terapijom po važećim preporukama. Bili su uključeni samo bolesnici sa koronarografi dokazanim reperfuzijom koronarne arterije. Istraživanjem nisu bili obuhvaćeni bolesnici sa akutnim i hroničnim inflamatornim oboljenjima, zatim bolesnici koji su na prijemu imali povisenu sedimentaciju (SE), fibrinogen, kreatinin-kinazu (CK) ≥ 190 U/L, kao ni oni sa ranim i kasnim kompleksijama AIM. C-reaktivni protein određivan je odmah po prijemu, potom 24, 48 i 72 sata, a nakon 21 dana, fibrinogen izrađen samo kod bolesnika sa IAM.
48, 72 sata nakon prijema, te 21. dana od hospitalizacije. Fibrinogen je određivan samo na prijemu. Rezultati. Na osnovu koronarografskog nalaza bolesnici su bili podeljeni u dve grupe: grupa 1 (23 bolesnika) bez značajne stenoze IA (stenoza ≥ 75%), i grupa 2 (13 bolesnika) sa značajnom stenozom IA (stenoza < 75%). Srednja vrednost CRP na prijemu u grupi 1 iznosila je 4,4 mg/L, a u grupi 2 7,2 mg/L (p < 0,001). Srednja vrednost CRP nakon 48 sati u grupi 1 bila je 21,7 mg/L, a u grupi 2 42,4 mg/L (nja vrednost CRP nakon 48 sati u grupi 2 je 5,5 mg/L (p < 0,001). Nakon tri nedelje vrednost CRP u grupi 1 bila je 4 mg/L, a u grupi 2 je 5,5 mg/L (p < 0,001 ). Grupe se statistički nisu razlikovale po polu, godinama, lokaciji AIM, vrednostima CK, EF i faktorima rizika od koronarne bolesti. Zakućaj. Kod bolesnika sa nesignifikantnom stenozom infarktna arterije postoji pojačan inflamatorni odgovor akutne faze. Ovo pokazuje da postoje različiti patogenetski mehanizmi u nastanku iste kliničke slike i/ili različite individualne reaktivnosti na inflamatorni stimulus.

Ključne reči: ateroskleroza; infarkt miokardia; inflamacija; koronarna arterija; stenoza; akutna bolest; c-reaktivni protein; fibrinogen.

Introduction
Atherosclerosis and coronary artery disease (CAD) as inflammatory diseases, set the new light on the pathogenesis of unstable angina pectoris (UA) and acute myocardial infarction (AMI) or acute coronary syndrome (ACS) 1-3. The most common causes of coronary thrombosis are endothelial erosion and rupture of atherosclerotic plaque 4. Rupture of plaque with a thin fibrous cap and large lipid core is more common in places with less narrowing of the lumen 4, while endothelial erosion mainly develops on plaque with a thick fibrous cap, and these plaques usually make big narrowing of coronary arteries 5,4. In both cases (rupture, erosion) the increased concentration of activated macrophages and T lymphocytes provide a greater endothelial loss (erosion), damage or rupture of the fibrous plaque cap, ie. active inflammatory process favors plaque instability 5-4. Angiographic studies 5 and data obtained by atherectomy of the coronary arteries in patients with ACS 6,7 and by autopsy of patients who died of sudden cardiac death, suggest that in pathogenesis of ACS an active inflammatory process in atherosclerotic plaques is more important than percent of coronary stenosis 6-9. In fact, inflammatory process determines plaque morphology and its stability 1. Inflammation, systemic or local, induces production of multipotential proinflammatory, primary cytokines, interleukin (IL) 1β, TNF-α. The primary cytokines stimulate the production of "mesenger" cytokine IL-6, which induces the expression of genes responsible for production of acute phase inflammation protein C-reactive protein (CRP) 10. Serum CRP concentration increases six hours after acute stimuli, the maximum value is recorded in the period 24–48 hours; its half-life in circulation is 19 h 11. High CRP serum concentration is associated with adverse prognosis of ACS 12, 13, and numerous prospective epidemiological studies have shown that elevated serum concentrations of CRP within the normal range (in the control group) is a predictor of future myocardial infarction or stroke 14. In studies that examined the acute phase response and kinetics of proinflammatory cytokines in patients after AMI, it was noticed that the intensity of acute phase response is in direct correlation with the size of infarction and the short- and long-term prognosis. However, in some of these studies, particularly those with thrombolytic therapy, there was no correlation between infarct size and intensity of acute phase response 15-17. This fact is extremely important, because it indicates that approximately the same active stimulus (plaque rupture and / or myocyte necrosis) in different patients induces various acute phase inflammatory response. This has been confirmed by a research in which inflammatory response in patients with AMI which was preceded by UA was compared to that in patients with AMI as the first manifestation of coronary heart disease 15. Enhanced inflammatory response in patients with preinfarction UA is consistent with earlier observations that in time of hospital admission an activation of monocytes was observed in patients with unstable angina but not in patients with AMI and stable angina pectoris 18. Also, some studies suggest that CRP serum level reflects inflammatory activity of plaque rupture and its morphology 15-16. In that context, the aim of our study was to determine the inflammatory state immediately preceding AMI as well as the correlation between serum concentrations of CRP and fibrinogen and infarct artery stenosis.

Methods
The study included 35 patients with AMI as the first manifestation of ischemic heart disease, indicated for thrombolytic therapy at an accelerated protocol for rt-PA, having in mind contraindications for this therapy 20. The survey did not include patients with CK values ≥ 190 U/L at admission, with clinically defined heart failure and echocardiographic estimated ejection fraction (EF) of less than 45%, those with early complications of AIM (postinfarction angina, reinfarction, periaditus), left bundle branch block and atrial fibrillation, and patients with diabetes mellitus. Also, the study did not include patients with acute infectious syndrome and other inflammatory diseases that are associated with increased acute phase response proteins, nor patients with neoplasms which were established by clinical and laboratory findings. We have not included patients with an elevated sedimentation rate (for women above 20, and for men more than 10), fibrinogen higher than 3,5 g/L, and leukocytosis (greater than 10x109 /L). All analysis were performed before the therapy, ie. at the admission. All the patients were treated with thrombolytic therapy with t-IPA in an accelerated protocol (15 mg in bolus, then 50 mg in an infusion for 30 minutes, and 35 mg for a period of sixty minutes). All the patients were receiving continuous infusion of heparin in the first 24 hours as well as intravenous infusion of nitroglycerin at a dose 0.8 mg/hour,
during the first 48 hours, and then isosorbidmononitrate. All the patients were receiving oral aspirin from the beginning of the treatment, and ACE-inhibitors from the second day of hospitalization. Twenty-eight patients were receiving beta-blockers, and three patients calcium antagonists.

Based on the coronaryographic findings, the patients were divided into two groups: the group 1 with significant stenosis of the infarct artery (≥ 75%); and the group 2 with nonsignificant stenosis of the infarct artery (< 75%) 21,22.

Serum CRP concentrations were determined by agglutination with monoclonal antibodies to CRP, and read out by nephelometric method. They were determined at admission (CRP0) and 24, 48 and 72 hours after admission, and on twenty-first day. CRP concentrations were determined by Behring Nephelometer 100 Analyzer (normal values 0–5 mg/L). Sedimentation rate was determined immediately upon admission of each patient, on a Monitor-S AUTO e.s.r. Analyzer. Serum fibrinogen concentration was determined immediately after admission in all patients, on a Behring Nephelometer Analyzer II (normal values 1.8 to 3.5 g/L). Leukocytes were determined from complete blood count on a Bayer-Technicon H * 3RTX device.

The concentration of CK was determined on admission, then every 6 hours in the first 24 hours, and twice daily on the second day and once daily till normalization of enzyme values (Hitachi 911 Automatic Analyzer; normal values 0–190 U/L). All analyses were performed at the Institute of Biochemistry, Military Medical Academy.

Left ventricular ejection fraction was determined by the method of Simpson. Coronary angiography examinations were performed at the Institute of Radiology, Military Medical Academy, and interpreted by the two independent experts.

For all parametric observations mean values and standard deviations were calculated. Statistically significant differences between individual parameters were calculated by the Student’s t-test. For nonparametric observations the frequency was determined and the differences were calculated by χ² test. A degree of correlation between each parameter was specified by linear correlation coefficient or by contingency coefficient. The significance of differences was accepted at 0.05.

**Results**

The study included 35 patients, 26 men and 9 women (ratio male : female, 3 : 1). The average age in the entire group was 55 years. The youngest patient was 31 and the oldest one 72.

On the basis of angiographically assessed stenosis of the infarct artery, patients were divided into two groups: the group 1 with significant stenosis (n = 22 patients); the average stenosis in the group was 86%, the lowest 75% and max 90%, the group 2 with nonsignificant stenosis (n = 13 patients); the average stenosis in the group was 47%, max. 70% and three patients did not have stenosis of infrarct-related artery. The percent of men and women in both groups was similar (77% and 69%, respectively).

The time from symptom onset till the administration of thrombolytic therapy was almost identical in both groups (107 and 108 minutes). The studied groups did not differ significantly in basic characteristics (gender, hypercholesterolemia, hypertension, family history of heart attack, localization of the infarction, the number of stenotic coronary arteries). Data on risk factors were obtained from the medical history and laboratory tests (Table 1). There was no statistically significant difference between the groups in age, EF, and the maximum values of CK (U/L; X ± SD). The group 1 – patient with coronary artery stenosis ≥ 75%.

The group 2 – patient with coronary artery stenosis < 75%.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr), X ± SD</td>
<td>57 ± 8.5</td>
<td>51 ± 10</td>
<td>0.68</td>
</tr>
<tr>
<td>Female sex, n/total n</td>
<td>5/17</td>
<td>4/9</td>
<td>0.60</td>
</tr>
<tr>
<td>Risk factors, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypercholesterolemia</td>
<td>11 (50%)</td>
<td>4 (31%)</td>
<td>0.27</td>
</tr>
<tr>
<td>hypertension</td>
<td>7 (32%)</td>
<td>3 (23%)</td>
<td>0.58</td>
</tr>
<tr>
<td>current cigarette use</td>
<td>14 (64%)</td>
<td>8 (62%)</td>
<td>0.9</td>
</tr>
<tr>
<td>family history of coronary artery disease</td>
<td>12 (55%)</td>
<td>4 (31%)</td>
<td>0.17</td>
</tr>
<tr>
<td>AIM location, n (%)</td>
<td></td>
<td></td>
<td>0.15</td>
</tr>
<tr>
<td>anterior</td>
<td>10 (45%)</td>
<td>6 (46%)</td>
<td></td>
</tr>
<tr>
<td>inferior</td>
<td>12 (55%)</td>
<td>5 (39%)</td>
<td></td>
</tr>
<tr>
<td>lateral</td>
<td>0</td>
<td>2 (15%)</td>
<td></td>
</tr>
<tr>
<td>The maximum values of CK (U/L; X ± SD)</td>
<td>1879 ± 1064</td>
<td>1661 ± 772</td>
<td>0.52</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>52 ± 5</td>
<td>52 ± 4</td>
<td>0.94</td>
</tr>
<tr>
<td>Incidence of the disease, n (%)</td>
<td>0.79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>single vessel</td>
<td>11 (50%)</td>
<td>8 (62%)</td>
<td></td>
</tr>
<tr>
<td>two vessel</td>
<td>6 (27%)</td>
<td>3 (23%)</td>
<td></td>
</tr>
<tr>
<td>three vessel</td>
<td>5 (23%)</td>
<td>2 (15%)</td>
<td></td>
</tr>
<tr>
<td>collaterals</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>The degree of stenosis of the infarct related artery (%)</td>
<td>86 ± 6</td>
<td>47 ± 27</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>min. stenosis</td>
<td>75%</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>max. stenosis</td>
<td>90%</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>The time interval from the beginning symptoms before the therapy (min), X ± SD</td>
<td>107 ± 32</td>
<td>108 ± 36</td>
<td>0.95</td>
</tr>
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</table>

Table 1

Clinical characteristics of patients with coronary artery stenosis
maximal levels of CK serum activity (table 1), as well as the sedimentation rate, leukocyte count, the values of CK on admission (Table 2). There was no correlation between the degree of stenosis and EF, extent of disease, localization of AMI, the time interval, SE, white blood cell count. There was a statistically highly significant difference between the two groups in the percentage of residual stenosis (p < 0.001).

At admission, elevated serum acute phase proteins, i.e. CRP and fibrinogen, were registered in 17 (48.6%) patients, 13 patients in the group 2, and only four (18%) patients in the group 1. In the group with significant stenosis of infarct artery (the group 1), the average value of CRP at admission (CRP0) was 4.4 mg/L, a minimum value 3 mg/L and a maximum value 6.6 mg/L. Of 22 patients, 18 (82%) had values of CRP0 within normal range, only four patients (18%) had values CRP0 more than normal (more than 5.0 mg/L) (Table 2). In the group 2 the average value CRP0 was 7.2 mg/L, a minimum value 5.7 mg/L, a maximum value 10.7 mg/L. All 13 patients had values CRP0 more than normal (Table 2).

Both groups showed an increase of CRP concentration with maximum value 48 hours after initiation of the therapy. Increased levels of CRP after three weeks were recorded in eight (23%) patients, and in the group 1, only in one patient (4.5%), and in the group 2 in seven (54%) patients (Figures 1 and 2). There was a statistically significant difference between the two groups in the CRP0 (p < 0.001), CRP values after 24 hours (p < 0.001), 48 hours (p < 0.001) and 72 hours (p < 0.002), and three weeks after AMI (p < 0.001) (Table 3, Figures 1 and 2).

Also, there was a very significant difference between the two groups in the values of fibrinogen at admission (p < 0.001) (Table 2). There was a statistically significant negative correlation between stenosis of the infarct artery and CRP0 value, CRP value after 24, 48, 72 hours and after three weeks (p < 0.001, p < 0.001, p < 0.01, p < 0.004, p < 0.003, respectively). Using the formula which links the maximum value of CRP and CK after AMI, for each patient the degree of inflammatory response (IO) was calculated 18: IO = (max. CRP value/max. CK value) x 100 According to this formale

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**Table 2**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Fibrinogen (g/L)</th>
<th>WBC (x10⁹)</th>
<th>ESR</th>
<th>CK (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>2.7 (2.1–3.1)</td>
<td>6.2 (4.9–7.8)</td>
<td>7 (2–16)</td>
<td>120 (86–168)</td>
</tr>
<tr>
<td>Group 2</td>
<td>3.0 (2.8–3.2)</td>
<td>5.8 (4.8–7.1)</td>
<td>6 (2–15)</td>
<td>105 (69–142)</td>
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<tr>
<td>&lt; 0.001</td>
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</table>

The group 1 – patient with coronary artery stenosis ≥ 75% The group 2 – patient with coronary artery stenosis < 75%
IO in the group 1 was 1.4 (± 0.6), and in the group 2 was 2.9 (± 0.7), (p < 0.001).

**Discussion**

The results show that about half of the patients (48.6%) with AMI as the first manifestation of CAD have a significantly enhanced response of acute phase proteins, i.e. CRP and fibrinogen. Acute phase response was significantly increased in all the patients with nonsignificant stenosis of the infarct artery (NSIA), in the group 2, and only in four (18%) patients in the group 1. The patients with NSIA (the group 2), totally 13 (37%), patients had much higher levels of CRP immediately after admission and also significantly higher levels of CRP after myocardial necrosis, and after three weeks (Table 3, Figure 1). Consistently, elevated levels of CRP in all patients with NSIA (the group 2), and only 4 (8%) patients in the group 1, are in accordance with other researches that found that for the occurrence of ACS more important is biological (inflammatory) state of the atherosclerotic plaque than the degree of coronary artery stenosis 3,23. The results are also consistent with earlier observations that AMI usually occurs with previously moderate stenosis of coronary artery 24,25, and after thrombolytic therapy, not a high number of infarct arteries are with high percent stenosis 5,6.

The study group (all 35 patients) was very homogeneous in terms of general characteristics (the first attack, the time interval until the beginning of the treatment, achieved reperfusion, ...). Also, between the groups, there were no statistically significant differences in gender, EF and other risk factors for CAD (Table 1).

In all the patients of the group with NSIA (the group 2), and in only 4 patients of the group 1, elevated levels CRP₀ and higher levels of fibrinogen (within the normal range) were found (Table 2).

Considering the facts that in all the patients from the onset of symptoms till administration of thrombolytic therapy passed less than two hours, and that acute stimuli lead to elevated levels of CRP after six hours (maximum values after 24–48 hours; half-life in circulation about 19 hours) 11, elevated levels of CRP₀ were not a result of myocardial necrosis (the levels of CK in all patients on admission were within normal range). Elevated levels of CRP on admission cannot be attributed to the severity and to the extent of atherosclerosis 26. In fact, the degree of atherosclerosis and acute phase response in patients with stable angina pectoris (SAP) and/or peripheral vascular disease, despite more extensive atherosclerosis and existence of thrombotic process, did not show a significant degree of correlation 26,27. CRP₀ higher values cannot be consequences of episodic activation of hemostatic system, because systemic markers of thrombin activation do not lead to elevation of acute phase protein 26,28 neither can be attributed to ischemia-reperfusion lesion, because the circulating neutrophils are not activated, and levels of CRP are not elevated in patients with a variant angina 29,30.

It cannot be excluded that a proportion of patients (but not the majority!) had silent ischaemia preceding AMI. However, in the group 2 in all the patients, and in the group 1 in 18% of the patients there was an increase of CRP₀, which limits this assumption. In addition, elevated CRP levels in the group 2 were maintained even after three weeks (5.5 mg/L compared to 4.0 mg/L in the group 1). CRP₀ higher values cannot be justified by acute infectious and/or other diseases, because erythrocyte sedimentation rate (ESR), fibrinogen and white blood cells (BC) were within normal values (Table 3). In addition to normal ESR, Le, BC, and, especially, fibrinogen support the hypothesis that myocardial infarction was not preceded by unrecognized ischemia 1,13. For elevated CRP₀ value is, most likely, responsible activation of inflammatory processes within the atherosclerotic plaque, which is consistent with the role of inflammation in the destabilization of the plaque 3,4. This process is not localized, but by the proinflammatory and messinger cytokines leads to the system response i.e. to the production of acute phase protein 1,18. Therefore, cytokine production occurs in the atherosclerotic plaque as a reflection of qualitative and quantitative (inflammatory) properties of the plaque, especially in active plaques that directly precipitate the ACS 3,17.

The inflammatory response may be an indicator of angiographically insignificant plaques which normally are more prevalent than the “bigger” plaques 31. Also, and as our research shows, “smaller” plaques are often the cause of AMI as the first manifestation of CAD 32, and more often lead to sudden occlusion of the vessel, among other factor, because they are in a lesser extent associated with the protective effects of collateral circulation. Coronary angiography cannot precisely visualize atherosclerotic plaques that narrow the lumen of less than 40%, however, such plaques have a “large” inflammatory potential 1,17. On the other hand, CRP may be a measure of individual reactions to the same stimulus, which is, in this case, the pathological substrate that leads to “the origin and development” of atherosclerotic plaque in coronary arteries. Actually, there is an interindividual difference in response to risk factors for CAD, as well as to antigens and autoantigenes that can lead to the development of atherosclerotic process 1,10,18.

Myocite necrosis is a potent proinflammatory stimulus 33,34. Experimental studies have shown that even brief periods of ischemia (15 minutes), after which follows reperfusion, cause a cascade of proinflammatory reactions that include: production of reactive oxygen metabolites (ROM) 35, leukocyte-mediated myocardial cell lesion 36 and cytokine IL-1 and Il-6, which are the main determinants for the production of acute phase proteins 1. Studies that examined the acute phase response and kinetics of proinflammatory cytokines in patients after AMI, have documented that the acute phase response is in direct correlation with the short and long term prognosis 12,13,37. However, in some of these studies, particularly those with early thrombolytic therapy, there was no correlation between infarct size and acute phase response 15,16. Our data show a typical increase in acute phase proteins after myocardial necrosis, with maximum values 48 hours after the thrombolytic therapy, which is in accordance with the mentioned studies (Table 3). Acute phase response was markedly higher in patients with NSIA (the group 2 with a mean CRP 42.4 mg/L compared to 21.7 mg/L in the group

putting aside the degree of stenosis of coronary arteries. In crucial pathological substrate in the development of ACS, be useful but have their limitations. Mography and magnetic resonance imaging have proved to apparent, but this invasive method is coupled with a significant, which causes ACS, cannot be determined by any currently available method. Intracoronary ultrasound detects unstable plaque in patients with NSIA could be induced to produce more cytokines and ROM on similar stimuli. These results are consistent with similar studies that compared inflammatory response in the patients with unstable angina and AMI (as the first manifestations of CAD 18, and with the observations that a proportion of patients have an elevated activity (measured with CRP) after uncomplicated angiography or PCI 40,41. The theory of increased individual reactivity to the stimulus (autoantigen, viruses, bacteria, inflammatory molecules) could explain the fact that one group of patients experience the first myocardial infarction without significant stenosis of the infarct artery.

The exact, in vivo, morphology of an inflamed plaque, which causes ACS, cannot be determined by any currently available method. Intracoronary ultrasound detects unstable plaque in patients with UA, which are angiographically inapparent, but this invasive method is coupled with a significant risk. Extravascular ultrasound, ultrafast computed tomography and magnetic resonance imaging have proved to be useful but have their limitations.

Contemporary concepts, based on molecular cardiology, favor the concept of vulnerable or inflamed plaque, as a crucial pathological substrate in the development of ACS, putting aside the degree of stenosis of coronary arteries. In our study, by following CRP kinetics in the first days of AMI, and compared with the degree of infarct artery stenosis, we detected a group of patients with elevated CRP and nonsignificant infarct artery stenosis.

The results of the study suggest two things: a) insignificant stenosis in a relatively large number precipitates development of AIM, b) insignificant stenosis of infarct-related artery is associated with enhanced inflammatory response. The object of our interest in this paper was not the prognosis of these patients in the context of coronaryographic findings and CRP. We had a special interest for the kinetics and strength of the acute-phase response in selected patients. Arising from the research results, and based on the experience of others authors, we believe that inflammation plays an important role in the prognosis of CAD, but more as individual than a group character. In fact, markers of the inflammatory milieu, and the inflammation itself, local and/or systemic, are determinants that show “rate of development of atherosclerosis and its complications”, favoring the occurrence of ACS in younger patients and making plaque “more atheromatous and less fibrous”.

However, from a clinical point of view, both morphologic forms (nonsignificant and significant stenosis of coronary arteries) lead to myocardial infarction, and in this context periprocedural serum concentration of CRP lost significance. Namely, heart attack develops in patients with elevated, as well as in those with normal CRP values. In this context, the value of CRP may have significance if it is compared with the clinical outcome of patients after definitive care (medical therapy, percutaneous coronary revascularization or surgical implantations). In fact, preprocedural value of CRP may help in deciding on the modalities of treatment 42.

Conclusion

Patients with nonsignificant stenosis of infarct-related artery had increased inflammatory responses according to the CRP value, as result of inflammatory process in atherosclerotic plaque and/or enhanced individual reactivity.

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