Clin. Cardiol. 24, 615–619 (2001)

C-Reactive Protein as a Risk Factor for Left Ventricular Thrombus in Patients with Acute Myocardial Infarction

ŞÜKRÜ ÇELIK, M.D., MERIH BAYKAN, M.D., CEVDET ERDÖL, M.D., KAĞAN KILINÇ, M.D.,* ASIM ÖREM, M.D.,* CIHAN ÖREM, M.D., İSMET DURMUS, M.D.

KTÜ Faculty of Medicine, Department of Cardiology, and *Department of Biochemistry, Trabzon, Turkey

Summary

Background: Elevated C-reactive protein (CRP) has been found to correlate with higher risk for cardiac events in patients with acute myocardial infarction (AMI). It has been suggested that CRP may be involved in initiation process of coagulation; however, the role of CRP level in the formation of left ventricular (LV) thrombus has not been studied.

Hypothesis: This study investigated whether CRP is a risk factor for LV thrombus in patients with AMI.

Methods: Clinical, echocardiographic, and biochemical data were analyzed in 141 consecutive patients (aged 57 ± 13 years; 33 women) with first anterior AMI. Two-dimensional and Doppler echocardiographic examinations were performed on Days 1, 3, 7, 15, and 30. Blood samples were obtained every day during hospitalization. Serum CRP concentrations were measured by an ultrasensitive immunonephelometry method.

Results: Left ventricular thrombus was detected in 33 (23.4%) patients. Univariate analysis showed that patients with LV thrombus had a higher peak creatine kinase (CK) level (2879 ± 742 vs. 1693 ± 1210 I/U, p = 0.001), higher peak CRP level (14.9 ± 7.1 vs. 9.2 ± 6.8 mg/dl, p = 0.001), higher wall motion score index (1.8 ± 0.2 vs. 1.5 ± 0.3, p = 0.002), higher apical wall motion score index (2.35 ± 0.72 vs. 2.07 ± 0.70, p = 0.001), larger end-diastolic volume (145.2 ± 43.7 vs. 116.5 ± 44.2 ml, p = 0.002), larger end-systolic volume (85.4 ± 37.2 vs. 62.9 ± 31.6 ml, p = 0.003), and lower ejection fraction (42.1 ± 12 vs. 47.3 ± 13, p = 0.04). In multivariate analyses, only peak CK level (p = 0.0001), LV apical wall motion score index (p = 0.001), and CRP levels (p = 0.001) were independent predictors of LV thrombus formation.

Conclusions: These results suggest that CRP is a risk factor for LV thrombus in patients with AMI.

Key words: C-reactive protein, acute myocardial infarction, left ventricular thrombus

Introduction

Left ventricular (LV) thrombus is a frequent complication of acute myocardial infarction (AMI). Combining the results of the most important echocardiographic studies in a total of 2,018 patients, Dantzig *et al.*[1] reported a frequency of LV thrombus after AMI to be 27%. Several factors are associated with thrombus formation. Thrombus was found almost exclusively in anterior wall infarction.[1] Higher mortality has been reported in patients with LV thrombus after infarction,[2] especially when developing within the first 48 h after infarction.[3]

C-reactive protein (CRP) is a sensitive, nonspecific acute phase reactant. Its secretion is induced by cytokines, especially interleukin-6, which is produced by hepatocytes and activated macrophages.[4,5] Increased CRP levels are associated with a worse outcome among patients with a first AMI.[6] It has been reported that peak CRP >20 mg/dl is predictive for cardiac rupture, irrespective of infarct size.[7] Pietilä *et al.*[8] reported that the post-AMI rise of CRP was higher in patients dying within 6 months after AMI. It has been suggested that CRP may be involved in the initiation process of coagulation by inducing monocytes to express a membrane-bound glycoprotein: tissue factor; consequently, CRP might increase the risk of thrombosis.[9] The aim of this study was to investigate whether CRP is a risk factor for LV thrombus formation in patients with AMI.

Methods

Study Patients

Between April 1999 and June 2000, we have prospectively evaluated 141 consecutive patients with a first anterior wall AMI who met the following criteria: (1) Chest pain lasting >30 min, (2) ST-segment elevation >2 mm in at least two anterior electrocardiographic (ECG) leads, and/or (3) transient

Address for reprints:

Dr. Şükrü Çelik
KTÜ Faculty of Medicine
Department of Cardiology
61080 Trabzon, Turkey
e-mail: ercevdet@usa.net

Received: August 25, 2000
Accepted with revision: January 22, 2001

elevation of creatine kinase (CK) and/or MB isoenzyme. Patients with concomitant systemic diseases (cancer, rheumatic diseases, chronic liver disease, renal disorders, sepsis, and other infectious diseases) were excluded, as were patients with previous myocardial infarction. The majority of patients were male (n = 108; 77%) and their mean age was 57 ± 13 years. Clinical evaluation, ECG, blood pressure, and routine blood sampling were performed every day during hospitalization.

Thrombolytic therapy was administered in 88 of 141 (63%) patients. Of these, 34 received streptokinase (1,500,000 IU intravenously [IV] over 1 h) and 54 had recombinant tissue-type plasminogen activator (rTPA) (100 mg IV over 90 min). The administration of both thrombolytics was immediately followed by heparin: a 5,000 IU bolus followed by a continuous infusion (1,000 IU/h) for 2 days and then low-molecular-weight heparin during hospitalization. Fifty-three patients received no thrombolytic therapy because of late admission after the onset of the pain or some contraindication for thrombolysis. Of these, 49 received IV heparin (a 5,000 IU bolus and then 1,000 IU/h) for 2 days, followed by low-molecular-weight heparin during hospitalization. Antiplatelet therapy with aspirin (300 mg) was started on the first day of treatment in all patients. Oral anticoagulation was started in 33 of 141 patients because of the presence of LV thrombus detected by echocardiography (target International Normalized Ratio = 2–3). Of the 141 patients, 118 (84%) received an angiotensin-converting enzyme (ACE) inhibitor.

Echocardiograms

Patients were serially evaluated by two-dimensional and Doppler echocardiography in the following sequence: on admission (Day 1), and on Days 3, 7, 15, and 30. All examinations were performed with an HP SONOS 5500 machine, using a 2.5 MHz transducer (Agilent Technologies, Andover, Mass., USA).

The diagnosis of LV thrombus was made when an echodense mass with a margin distinct from the LV wall was detected within the LV cavity and was visible throughout the cardiac cycle in at least two different echocardiographic views and associated with asynergy (akinesis or dyskinesis) of the adjacent myocardium.[10]

Left ventricular end-diastolic and end-systolic volumes and ejection fraction were determined from apical two- and four-chamber view using the Simpson's biplane formula, according to the recommendations of the American Society of Echocardiography.[11] Tracing of endocardial borders in end diastole and end systole was performed in the technically best cardiac cycle.

To calculate the wall motion score index (WMSI), the left ventricle was divided into 16 segments.[11] Segmental wall motion was graded as follows: normal motion at rest (score = 1); hypokinetic—marked reduction in endocardial motion and systolic thickening (score = 2); akinetic—virtual absence of inward motion and systolic thickening (score = 3); and dyskinetic—paradoxical wall motion away from the center of the left ventricle in systole (score = 4). The WMSI was calculated by summation of individual segment scores divided by the number of interpreted segments. Each echocardiographic study was interpreted independently by two echocardiographers who were blinded to the patients' clinical and laboratory data. Inter-and intraobserver variability analysis was performed in 30 randomly chosen patients and was found to be $<5\%$ for all echocardiographic variables.

Blood Sampling and Assays

Venous blood samples were collected daily during hospitalization and kept at 4°C. Plasma or serum was separated within 2 h. Serum was assayed for CRP by particle-enhanced immunonephelometry with the Behring Nephelometer Systems Kit (N latex CRP mono, Behring, Germany). Polystyrene particles coated with mouse monoclonal antibodies to CRP were agglutinated when mixed with samples containing CRP. Serum CRP concentrations were measured by an ultrasensitive immunonephelometry method. Plasma fibrinogen level was measured by immunonephelometry using a commercial original kit (Dade Behring, Liederbach, Germany).

Statistical Analysis

Data are presented as mean ± standard deviation. A comparison between groups was performed by means of an unpaired *t*-test for continuous variables. Categorical variables were analyzed with contingency tables using the chi-square test and Fisher's exact test when appropriate. Pearson's correlation analysis was performed to estimate the correlation between variables. Multivariate logistic regression analysis was performed to identify the independent predictors of LV thrombus. For multiple regression, factors showing a value $p<0.1$ in univariate analysis were selected. A p value of <0.05 was considered statistically significant.

Results

Study Patients

Left ventricular thrombus was detected in 33 (23.4%) of 141 patients with AMI. All but one thrombi were localized in the LV apex, and almost all thrombi (31/33) were detected within the first week after infarction; only two thrombi were detected for the first time 4 weeks after infarction. According to LV thrombus formation, patients were assigned to the following two groups: Group 1, with LV thrombus (33 patients, 23.4%), Group 2, without LV thrombus (108 patients, 76.6%).

Patients' baseline characteristics are shown in Table I. Comparing patients with and without LV thrombus, there were no significant differences in age, gender, therapy, and risk factors for atherosclerosis, such as family history, cholesterol, diabetes, and smoking. Smoking, defined as current smoking, was present in 25 patients (77%) with thrombus and 78 patients (73%) without thrombus. There was no significant difference between patients with and without LV thrombus in the use of ACE inhibitors, heparin, and thrombolytics. The lipid profiles of the two groups, total cholesterol, low-density

TABLE I Baseline characteristics of study participants

	Thrombus (n = 33)	No thrombus (n = 108)	p Value[a]
Age, years	55 ± 12	58 ± 13	NS
Sex, % male	78	76	NS
Smoking, (%)	77	73	NS
Hypertension, (%)	35	36	NS
Diabetes, (%)	10	13	NS
Family history, (%)	46	53	NS
CRP, mg/dl	14.9 ± 7.1	9.2 ± 6.8	0.001
Fibrinogen, mg/dl	452 ± 235	427 ± 125	NS
Peak CK (U/l)	2769 ± 641	1706 ± 1138	0.001
Cholesterol, mg/dl	184 ± 32	188 ± 37	NS
HDL- cholesterol, mg/dl	35 ± 8	36 ± 10	NS
LDL- cholesterol, mg/dl	119 ± 34	125 ± 32	NS
Thrombolysis (%)	60	64	NS
ACE inhibitor (%)	79	85	NS
Heparin (%)	93	98	NS
Time from chest pain onset to thrombolysis	4.04 ± 2.1	4.73 ± 1.9	NS

[a] P values were obtained by chi-square test or Fisher's exact test for categoric variables and unpaired *t*-test for continuous variables. Values are mean ± standard deviation or percentages.

Abbreviations: CK = creatine kinase, CRP = C-reactive protein, HDL = high-density lipoprotein, LDL = low-density lipoprotein, ACE = angiotensin-converting enzyme, NS = not significant.

lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) are shown in Table I. No significant differences were found. The peak CK level was significantly higher in patients with than in those without LV thrombus (2769 ± 641 vs. 1706 ± 1138 I/U, p = 0.001). The two groups were similar regarding the fibrinogen level.

C-Reactive Protein Levels and Left Ventricular Thrombus Formation

The CRP levels were significantly higher in patients with than in those without LV thrombus (14.9 ± 7.1 vs. 9.2 ± 6.8 mg/dl, p = 0.001). There were no significant correlations between CRP levels and peak CK levels (r = −0.005, p = 0.9) and LV WMSI (r = −0.006, p = 0.8). A weak inverse correlation was found between CRP levels and LV ejection fraction (r = −0.213, p = 0.02). There were higher peak CRP levels in patients who had a history of smoking and diabetes than in those who did not, but this difference was not statistically significant (Table II). We subdivided our study population in quartiles of C-reactive protein (<4.37, 4.37–9.65, 9.65–15.75, and > 15.75). This stratification revealed an increased probability of LV thrombus occurrence in patients with increased C-reactive protein levels: 3, 20, 29, and 43%, respectively (p = 0.005, relative risk 3.45, confidence interval 1.42 to 8.3) (Fig. 1).

The echocardiographic data of the groups are presented in Table III. Patients in Group 1 had significantly larger LV end-

TABLE II Comparison of peak C-reactive protein (CRP) levels in patients with acute myocardial infarction by clinical status

	CRP levels (mg/dl)	Percentage of patients
Age < 45	9.6 ± 7.8	20
Age > 45	10.8 ± 7.1	80
Men	10.6 ± 7.6	76
Women	10.1 ± 7.1	24
Smoking habit	11.2 ± 6.8	75
No smoking habit	9.4 ± 5.1	25
Hypertension	10.3 ± 7.2	36
No hypertension	11.3 ± 7.4	64
Diabetes mellitus	12.4 ± 8.3	12
No diabetes mellitus	10.3 ± 7.5	88

There was no significant difference between plasma levels of CRP. Values are mean ± standard deviation or percentages. P values were obtained by unpaired *t*-test for continuous variables.

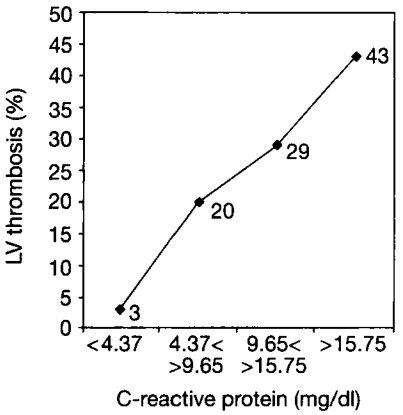

FIG. 1 Distribution of left ventricular (LV) thrombi per quartile of C-reactive protein. Patients with C-reactive protein values > 15.75 mg/dl had a higher incidence of LV thrombi (p = 0.005, relative risk 3.45, confidence interval 1.42 to 8.3) than the other groups.

TABLE III Echocardiographic characteristics in patients with and without left ventricular thrombus

	Thrombus (n = 33)	No thrombus (n = 108)	p Value
WMSI	1.8 ± 0.2	1.5 ± 0.3	0.002
Apical WMSI	2.35 ± 0.72	2.07 ± 0.70	0.001
LVEDV, ml	145.2 ± 43.7	116.5 ± 44.2	0.001
LVESV, ml	85.4 ± 37.2	62.9 ± 31.6	0.003
EF (%)	42.1 ± 12	47.3 ± 13	0.04

Values are mean ± standard deviation or percentages.

Abbreviations: WMSI = wall motion score index, EF = ejection fraction, LVEDV = left ventricular end-diastolic volume, LVESV = left ventricular end-systolic volume.

TABLE IV Multivariate regression analysis for left ventricular thrombus in patients with acute myocardial infarction

	p Value
CRP	0.001
Peak CK	0.0001
Apical WMSI	0.001
WMSI	NS
LVEDV	NS
LVESV	NS
EF	NS

Abbreviations as in Tables I and II.

diastolic and end-systolic volume, and higher WMSI than patients in Group 2. The LV ejection fraction was significantly lower in Group 1 than in Group 2. To assess whether CRP levels were independently related to the increased risk of LV thrombus formation, logistic regression analysis was performed with other risk factors also taken into account. Multivariate analyses showed that peak CK level ($p = 0.0001$), LV WMSI ($p = 0.001$), and CRP levels ($p = 0.001$) were independent predictors of LV thrombus formation (Table IV).

Discussion

In this study, we found that elevated levels of CRP were associated with increased risk of LV thrombus formation in patients with acute anterior MI. To our knowledge, this study is the first report to investigate a relation between the CRP levels and LV thrombus in patients with AMI.

The incidence of LV thrombi in our study (23.4%) was slightly lower than previously reported,[1] possibly due to changes in AMI management. The frequent use of reperfusion may have reduced the incidence of LV thrombus. Moreover, in our study all patients underwent systemic thrombolysis, if not contraindicated, immediately followed by anticoagulation with IV heparin. The majority of the remaining patients received IV heparin and ACE inhibitor.

C-Reactive Protein and Cardiovascular Disease

Inflammation plays a significant role in the pathogenesis of cardiovascular disease.[12–14] C-reactive protein is a sensitive marker of inflammation. Initially, Liuzzo *et al.*[15] and Haverkate *et al.*[16] established the prognostic usefulness of CRP in the setting of angina. With the use of new, sensitive CRP assays, CRP was identified as an independent, prospective cardiovascular risk factor in the higher-risk, middle-aged men of the Multiple Risk Factor Intervention Trial (MRFIT).[17] In cardiovascular disease without myocardial necrosis (atherosclerosis and stable and unstable angina), plasma CRP levels correlate with the extent and severity of atherosclerosis.[18] It has been demonstrated that CRP increases in acute coronary syndromes (unstable angina and AMI) and that it is associated with an adverse outcome regarding both in-hospital course[6] and long-term prognosis.[8, 19] It has been reported that peak CRP > 20 mg/dl is predictive for cardiac rupture, irrespective of infarct size.[7] In our study, elevated CRP levels were associated with an increased probability of LV thrombus development.

Relation of C-Reactive Protein to Thrombus Formation

As a marker of inflammation, CRP is unique among the major plasma proteins because its levels appear to be unaffected by hormones and anti-inflammatory drugs, but are regulated primarily by the proinflammatory cytokines, such as interleukin-6.[20] The accumulation of CRP and activated complement fragments in infarcted myocardium has been demonstrated in postmortem studies.[21] Plasma CRP increases markedly during acute phase reactions, including AMI.[22–24] The physiologic role of CRP is yet unknown. In vitro, CRP shows both proinflammatory and anti-inflammatory effects.[25, 26] The former include the ability of ligand-bound CRP to activate the complement system.[26] Activation of the classic pathway of complement by ischemic myocardium has been demonstrated in various animal models for AMI.[27, 28] Also in humans, the complement is activated by ischemic myocardium.[21, 28, 29] Activation of the complement fragments may induce vascular and myocardial damage through various mechanisms: stimulation, aggregation, and degranulation of neutrophils;[30] enhancement of clotting by induction of tissue factor expression and the formation of procoagulant microvesicles;[31, 32] or even direct damage of endothelial cells and cardiomyocytes by insertion of pores (C5b-9) into the cell membrane.[32] Consequently, thrombus formation increases.

Previous echocardiographic studies investigating the correlation between post-AMI rise of CRP and infarct size revealed conflicting results: Several studies reported that postacute myocardial infarction rise of CRP correlates with infarct size;[33] however, some studies showed no correlation between CRP levels and infarct size in patients with AMI.[34, 35] In this study, we found a weak negative correlation between CRP level and LV ejection fraction in patients with AMI.

Several factors are associated with LV thrombus formation after AMI. Most studies found an association of thrombus with increased enzymatic infarct size, clinical evidence of pump failure, severe apical asynergy, increased LV volumes, and decreased global LV function.[36, 37] In our study we also found that LV thrombus formation was associated with a higher end-systolic volume, a higher WMSI, a lower initial ejection fraction, and a higher peak CK level.

Conclusion

According to these findings, increased CRP is a risk factor for LV thrombus formation in patients with AMI. Therefore, assays of CRP values may contribute to more complete risk stratification after a first myocardial infarction. The most important limitation of our study involves the small number of patients studied because of the selective criteria for inclusion into the study. Large prospective studies are needed to establish the CRP level as a risk factor for LV thrombus formation in AMI.

References

1. Dantzig JMV, Delemarre BJ, Bot H, Visser CA: Left ventricular thrombus in acute myocardial infarction. *Eur Heart J* 1996;17: 1640–1645
2. Friedman MJ, Carlson K, Marcus FI, Woolfenden JM: Clinical correlations in patients with acute myocardial infarction and left ventricular thrombus detected by two-dimensional echocardiography. *Am J Med* 1982;72:894–898
3. Spirito P, Belloti P, Chiarella F, Domenicucci S, Sementa A, Vecchio C: Prognostic significance and natural history of left ventricular thrombi in patients with acute anterior myocardial infarction: A two-dimensional echocardiographic study. *Circulation* 1985;72:774–780
4. Haverkate F, Thompson SG, Pyke SDM, Gallimore JR, Pepys MB: Production of C-reactive protein and risk of coronary events in stable and unstable angina. *Lancet* 1997;349:462–466
5. Pannitteri G, Marino B, Campa PP, Martucci R, Testa U, Peschle C: Interleukins 6 and 8 as mediators of acute phase response in acute myocardial infarction. *Am J Cardiol* 1997;80:623–625
6. Anzai T, Yoshikawa T, Shiraki H, Asakura Y, Akaishi M, Mitamura H, Ogawa S: C-reactive protein as a predictor of infarct expansion and cardiac rupture after a first Q wave acute myocardial infarction. *Circulation* 1997;96:778–784
7. Ueda S, Ikeda U, Yamamoto K, Takahashi M, Nishinaga M, Nago N, Shimada K: C-reactive protein as a predictor of cardiac rupture after myocardial infarction. *Am Heart J* 1996;131:857–860
8. Pietilä KO, Harmoinen AP, Jokiniitty J, Pasternac AI: Serum C-reactive protein concentration in acute myocardial infarction and its relationship to mortality during 24 months of follow-up in patients under thrombolytic treatment. *Eur Heart J* 1996;17:1345–1349
9. Linnanmäki E, Leinonen M, Mattila K, Nieminen MS, Valtonen V, Saikku P: Chlamydia pneumoniae-specific circulating immune complexes in patients with chronic coronary heart disease. *Circulation* 1993;87:1130–1134
10. Asinger RW, Mikell FL, Elsperger J, Hodges M: Incidence of left ventricular thrombosis after acute transmural myocardial infarction: Serial evaluation by two-dimensional echocardiography. *N Engl J Med* 1981;305:297–302
11. Schiller N, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, Gutgesell H, Reichek N, Sahn D, Schnittger I: Recommendation for quantitation of the left ventricle by two dimensional echocardiography. *J Am Soc Echocardiogr* 1989;2:358–368
12. Ross T: The pathogenesis of atherosclerosis: A perspective for the 1990s. *Nature* 1993;362:801–809
13. Libby P: Molecular basis of the acute coronary syndromes. *Circulation* 1995;91:2844–2850
14. Ridker PM: C-reactive protein and risk of future myocardial infarction and thrombotic stroke. *Eur Heart J* 1998;19:1–3
15. Liuzzo G, Biasucci LM, Gallimore JR, Grillo RL, Rebuzzi AG, Pepys MB, Maseri A: The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. *N Engl J Med* 1994;331:417–424
16. Haverkate F, Thompson S, Duckert F: Haemostasis factors in angina pectoris: Relation to gender, age and acute-phase reaction. *Thromb Haemost* 1995;73:561–567
17. Kuller LH, Tracy RP, Shaten J, Meilahn EN: Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study. *Am J Epidemiol* 1996;144:537–547
18. Heinrich J, Schulte H, Schönfeld R, Köhler E, Assmann G: Association of variables of coagulation, fibrinolysis and acute-phase with atherosclerosis in coronary and peripheral arteries and those arteries supplying the brain. *Thromb Haemostas* 1995;73:374–378
19. Toss H, Lindahl B, Siegbahn A, Wallentin L: Prognostic influence of increased fibrinogen and C-reactive protein levels in unstable coronary artery disease. *Circulation* 1997;96:4204–4210
20. Pepys M: C-reactive protein fifty years on. *Lancet* 1981;i:653–656
21. Lagrant WK, Niessen JWM, Wolbink GJ, Jaspars EH, Visser CA, Verheugt FWA, Meijer CJLM, Hack CE: C-reactive protein colocalizes with complement in human hearts during acute myocardial infarction. *Circulation* 1997;95:97–103
22. Agrawal A, Kilpatrick JM, Volanakis JE: Structure and function of human C-reactive protein. In *Acute Phase Proteins. Molecular Biology, Biochemistry, and Clinical Applications* (Eds. Mackiewicz A, Kushner I, Baumann H), p. 19–92. Boca Raton, Fla: CRC Press, Inc., 1993
23. de Beer FC, Hind CRK, Fox KM, Allan RM, Maseri A, Pepys MB: Measurement of serum C-reactive protein concentration in myocardial ischaemia and infarction. *Br Heart J* 1982;47:239–243
24. Pietilä KO, Harmoinen AP, Hermens WT, Simoons ML, van de Werf F, Verstraete M: Serum C-reactive protein and infarct size in myocardial infarct patients with a closed versus an open infarct-related coronary artery after thrombolytic therapy. *Eur Heart J* 1993;14:915–919
25. Heuertz RM, Piquette CA, Webster RO: Rabbits with elevated serum C-reactive protein exhibit diminished neutrophil infiltration and vascular permeability in C5a-induced alveolitis. *Am J Pathol* 1993;142:319–328
26. Volanakis JE: Complement activation by C-reactive protein complexes. *Ann N Y Acad Sci* 1982;389:235–249
27. Kilgore KS, Friedrichs GS, Homeister JW, Lucchesi BR: The complement system in myocardial ischemia/reperfusion injury. *Cardiovasc Res* 1994;28:437–444
28. Pinckard RN, Olson MS, Giclas PC, Terry R, Boyer JT, O'Rourke RA: Consumption of classical complement components by heart subcellular membranes in vitro and in patients after acute myocardial infarction. *J Clin Invest* 1975;56:740–750
29. Mathey D, Schofer J, Schäfer HJ, Hamdoch T, Joachim HC, Ritgen A, Hugo F, Bhakdi S: Early accumulation of the terminal complement-complex in the ischaemic myocardium after reperfusion. *Eur Heart J* 1994;15:418–423
30. Engler RL, Schmid-Schonbein GW, Pavelec RS: Leukocyte capillary plugging in myocardial ischemia and reperfusion in the dog. *Am J Pathol* 1983;111:98–111
31. Carson SD, Johnson DR: Consecutive enzyme cascades: Complement activation at the cell surface triggers increased tissue factor activity. *Blood* 1990;762:361–367
32. Hamilton KK, Hattori R, Esmon CT, Sims PJ: Complement proteins C5b-9 induce vesuculation of the endothelial plasma membrane and expose catalytic surface for the assembly of the prothrombinase enzyme complex. *J Biol Chem* 1990;256:3809–3814
33. Lagrand WK, Viser CA, Hermens WT, Niessen HW, Verheugt FW, Wolbink GJ, Hack CE: C-reactive protein as a cardiovascular risk factor. *Circulation* 1999;100:96–102
34. Tommasi S, Carluccio E, Bentivoglio M, Buccolieri M, Mariotti M, Politano M, Corea L: C-reactive protein as a marker for cardiac ischemic events in the year after a first, uncomplicated myocardial infarction. *Am J Cardiol* 1999;83:1595–1599
35. Pietilä K, Harmoinen A, Teppo A-M: Acute phase reaction, infarct size and in-hospital morbidity in myocardial infarction patients treated with streptokinase or recombinant tissue type plasminogen activator. *Ann Med* 1991;23:529–535
36. Arvan S: Left ventricular mural thrombi secondary to acute myocardial infarction: Predisposing factors and embolic phenomenon. *J Clin Ultrasound* 1983;11:467–473
37. Domenicucci S, Chiarella F, Bellotti P, Lupi G, Scarsi G, Vecchio C: Early appearance of left ventricular thrombi after anterior myocardial infarction: A marker of higher in-hospital mortality in patients not treated with antithrombotic drugs. *Eur Heart J* 1990; 11:51–58