Acute Ischemic Heart Disease

C-Reactive protein levels on admission are associated with response to thrombolysis and prognosis after ST-segment elevation acute myocardial infarction

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Background Several studies have shown the independent association of high plasma C-reactive protein (CRP) levels with an adverse prognosis in patients with acute myocardial infarction. However, the possible association of plasma CRP levels with response to thrombolysis and short- and long-term cardiac mortality has not been investigated. The aim of this study was to evaluate these possible associations.

Methods Three hundred nineteen consecutive patients who received intravenous thrombolysis because of ST-segment elevation acute myocardial infarction were prospectively studied. Patients were classified according to tertiles of plasma CRP levels on admission.

Results Patients at the top tertile had a significantly lower incidence of complete ST-segment resolution (third vs first, $P < .001$, third vs second, $P = .009$) or Thrombolysis In Myocardial Infarction (TIMI) 3 flow in the infraction-related artery (third vs first, $P < .001$, third vs second, $P = .02$), more compromised left ventricular function (third vs first, $P = .02$, second vs third, $P = .04$), greater inhospital mortality (third vs first, $P = .03$, third vs second, $P = .06$), and greater 3-year cardiac mortality (third vs first, $P = .01$, third vs second, $P = .07$).

Conclusions Plasma levels of CRP on admission may be a predictor of reperfusion failure and of short- and long-term prognosis in patients with ST-segment elevation acute myocardial infarction. (Am Heart J 2002;144:782-9.)

Rapid and adequate reperfusion of jeopardized myocardium constitutes the only effective treatment in patients with ST-segment elevation myocardial infarction (STEMI).[1,2] Early recanalization of the infraction-related artery results in the preservation of left ventricular systolic performance and subsequently in more favorable short- and long-term prognosis. Although the benefits of intravenous thrombolysis are unequivocal, reperfusion fails in a significant proportion of patients.[3,4] Beyond the well-established adverse influence of prehospital delay,[5] other factors such as antibodies to streptokinase[6] and individual characteristics of the culprit plaque[7,8] have been suggested as predictors of inadequate response to intravenous thrombolysis.

However, accumulating reports have expanded our knowledge on the pathogenesis of acute coronary syndromes, introducing the pivotal role of inflammation.[9]

Cardiovascular research has recently been attracted by the potential clinical implication of the role of inflammation, focusing on the identification of inflammatory markers, which could be easily detected and could contribute to the risk stratification in patients with coronary artery disease. C-Reactive protein (CRP) is a sensitive and nonspecific, cytokine-dependent[10] marker of inflammation and has received intense scrutiny.

Elevated plasma CRP levels detected in the first days of myocardial infarction (MI) may reflect an increased systematic inflammatory response, induced by myocardial necrosis,[11,12] and have been associated with unfavorable short- and long-term prognosis.[12-14] Intravenous thrombolysis has been reported to attenuate this

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response.[11,13] However, the possible relationship of plasma CRP levels, measured on admission, with the short- and long-term outcome of intravenous thrombolysis in patients with STEMI has not been thoroughly investigated. The aim of this prospective study was to investigate the possible association of plasma CRP levels on admission with the outcome of intravenous thrombolysis estimated by means of the incidence of either (1) complete ST-segment resolution 2 hours after thrombolysis initiation, or (2) Thrombolysis In Myocardial Infarction (TIMI) 3 flow in the infarction-related artery, and left ventricular ejection fraction (LVEF) assayed during hospitalization, as well as (3) inhospital and 3-year cardiac mortality.

Methods

Study population

The study cohort consisted of 339 consecutive patients with STEMI who were admitted at our institute from January 1998 to February 2000 and fulfilled these criteria: (1) continuous and present on admission, refractory to nitrates anginal chest pain of ≥30 minutes duration, (2) ST-segment elevation ≥2 mm in ≥2 contiguous precordial leads, or 1 mm in ≥2 contiguous limb leads, and (3) no contraindications to intravenous thrombolysis. Patients were excluded when they had (1) left bundle branch block or sustained tachycardia, (2) active infection or chronic inflammatory disease, (3) significant hepatic or renal dysfunction, (4) malignancy, (5) history of coronary bypass grafting surgery, or (6) MI or percutaneous coronary intervention in the last 6 months.

The local ethics committee approved the study protocol, and informed consent was obtained from all participants.

Collection of blood samples and CRP assay

On patient admission, venous blood samples were obtained before the intravenous administration of drugs. Coded plasma samples were stored at −24°C for CRP analysis the next day. The analysis of plasma CRP was performed by use of an immunonephelometric quantitative method (Turbicant, Dade Behring diagnostics, Marburg, Germany) covering a range of 0.5 to 60 mg/dL. For values below the limit of detection, the lower limit value was used for statistical analysis.

The higher normal limit for healthy nonpregnant adults was 0.5 mg/dL in the laboratory. CRP results were not decoded before the end of the study.

Treatment

The thrombolytic agent used was either streptokinase or t-PA. Chewable aspirin was given in a dose of 160 to 325 mg on admission and was continued indefinitely. Heparin was given as a bolus of 5000 units on admission, followed by intravenous infusion titrated to a therapeutic activated partial thromboplastin time. Heparin was continued in uncomplicated cases for 48 hours.

Complete ST-segment resolution and electrocardiographic analysis

Complete ST-segment resolution was considered to be a ≥70% reduction of the sum of ST-segment elevation[15] between the electrocardiogram on admission in the coronary care unit and the electrocardiogram 2 hours after thrombolysis initiation, as predefined by means of the protocol. All electrocardiograms were analyzed as pairs by 2 experienced cardiologists who were blinded to the patient data. The sum of ST-segment elevation was measured 20 ms after the end of the QRS complex in leads I, aVL, and V_1 to V_6 for anterior, and leads II, III, aVF, and V_5, V_6 for nonanterior MI.

Cardiac catheterization, TIMI flow, and LVEF

All catheterizations were performed via the femoral approach by use of the Seldiger technique during the first few days of the patient's hospitalization. Flow in the culprit arteries was graded according to the TIMI criteria.[16] LVEF was quantified by means of a standard technique from a single-plane projection in the 30 degree right anterior oblique view.[17] TIMI flow and LVEF were estimated by 2 experienced and independent angiographers who were blinded to the study. LVEF values were calculated as the mean score given by the 2 observers. In the case of disagreement between the observers in the classification of TIMI flow, it was estimated by means of consensus.

Clinical follow-up

Inhospital and postdischarge follow-up data were prospectively collected on predesigned case report forms. Before discharge, all patients were advised on smoking cessation, body weight reduction, regular exercise, and lipid monitoring. After discharge, patients were followed-up at 30 days and subsequently every 6 months on an outpatient basis or by means of telephone interview. Cardiac death was the prespecified primary end point. Cardiac death was considered to be any incidence of sudden unexplained death, death caused by fatal MI, and death after rehospitalization because of heart failure or possible acute myocardial ischemia.[18]

Statistical analysis

Values were expressed as the mean ± SD for normally distributed CRP values and as the median with 25th and 75th percentiles for non-normally distributed CRP values. Comparisons of continuous variables among CRP tertiles were made by use of analysis of variance (ANOVA) or the Kruskal-Wallis test, as appropriate. The Bonferroni in ANOVA or Mann-Whitney U test was used, as appropriate, for pairwise comparisons of continuous variables between tertiles. Associations between 2 categorical variables were tested by means of the χ^2 or Fisher exact tests, as appropriate. Nonparametric Spearman's r was used for correlations between non-normally distributed variables.

Interobserver agreement for the estimation of noninvasive and invasive indices of reperfusion was tested by means of the Cohen kappa method.

Univariate and multivariate logistic regression analyses were conducted as a means of estimating the univariate and multivariate predictors of noninvasive or invasive indices of

Table I. Comparison of baseline data among tertiles of CRP

	First (I) (n = 110)	Second (II) (n = 103)	Third (III) (n = 106)	P
CRP median (25th, 75th percentiles) mg/dL	0.5 (0.5, 0.52)	0.82 (0.6, 1.62)	2.98 (2.26, 4.21)	
Age (y)*	57.3 ± 10.6	61.3 ± 9.9	61.2 ± 11.1	.007
Males (%)†	80.9	71.8	67.9	.08
BMI ($kg.m^{-2}$)	27.5 ± 4.2	27.1 ± 3.1	26.9 ± 3.2	.43
Hypertension (%)	39.1	39.8	49.1	.26
Current smoking (%)‡	72.7	56.3	55.7	.01
Diabetes mellitus (%)	18.2	26.2	26.4	.27
Family history of CAD (%)§	41.8	38.8	51.9	.14
Hypercholesterolemia (%)‖	50.9	63.1	67.0	.04
History of stable angina (%)¶	18.2	26.2	27.4	.23
History of MI (%)#	10.9	13.6	13.2	.81
History of PCI (%)#	9.2	11.7	11.0	.61
Time from onset of pain to thrombolysis administration in hours	4.3 ± 2.7	4.5 ± 3.0	4.4 ± 2.9	.81
Anterior STEMI (%)	60.0	55.3	54.7	.69
t-PA (%)	53.6	47.6	45.3	.45
Creatin kinase-MB on admission, IU/L	40.2 ± 19.4	41.7 ± 21.7	40.0 ± 16.8	.79

Values are mean ± SD or as given. *BMI,* Body mass index; *CAD,* coronary artery disease; *PCI,* percutaneous coronary intervention; *t-PA,* tissue type plasminogen activator.
*P = .02 for II versus I, and P = .02 for III versus I.
†P = .1 for II versus I, and P = .03 for III versus I.
‡P = .01 for II versus I, and P = .009 for III versus I.
§P = .06 for III versus II.
‖P = .07 for II versus I, and P = .01 for III versus I.
¶P = .1 for III versus I.
#Not in the last six months.

Table II. Comparison of noninvasive and invasive indices of reperfusion among tertiles of CRP

	First (I)	Second (II)	Third (III)	P
Noninvasive data	(n = 110)	(n = 103)	(n = 106)	
ΣST1-elevation (mm)	14.7 ± 7.9	14.6 ± 7.9	14.6 ± 8.0	.99
ΣST2-elevation (mm)*	5.4 ± 4.9	5.7 ± 5.7	7.7 ± 6.3	.005
Number of leads with ST elevation >1 mm	4.3 ± 1.7	4.2 ± 1.7	4.1 ± 1.4	.81
Patients with ≥70% ST resolution (%)†	60.0	52.4	33.0	<.001
Patients with 30%-69% ST resolution (%)	27.3	24.3	21.7	.63
Patients with <30% ST resolution (%)‡	12.7	23.3	45.3	<.001
Peak creatin kinase-MB levels, IU/L§	81.3 ± 59.7	113.6 ± 89.6	149.7 ± 108.2	<.001
Invasive data	(n = 92)	(n = 89)	(n = 89)	
From admission through inhospital angiography in days, mean ± SD (range)	4.7 ± 1.2 (2-7)	4.6 ± 1.3 (2-7)	4.5 ± 1.5 (1-7)	.53
Multivessel CAD (%)	73.9	79.8	73.0	.52
TIMI 3 flow in culprit artery (%)‖	79.3	59.6	41.6	<.001
LVEF(%)¶	43.5 ± 8.4	41.6 ± 8.3	38.9 ± 8.2	.001
Patients with LVEF <45% (%)#	46.7	47.2	64.0	.03

Values are mean ± SD or as given. Σ*ST1,* Sum of ST-segment elevations on first electrocardiogram; Σ*ST2,* sum of ST-segment elevations on second electrocardiogram.
*P = .008 for III versus I, and P = 0.03 for III versus II.
†P < .001 for III versus I, and P = 0.005 for III versus II.
‡P = .04 for II versus I, P = 0.001 for III versus II, and P < .001 for III versus I.
§P = .02 for II versus I, P = 0.01 for III versus II, and P < .001 for III versus I.
‖P = .004 for II versus I, P = 0.02 for III versus II, and P < .001 for III versus I.
¶P = .04 for III versus II, and P = 0.001 for III versus I.
#P = .02 for III versus II, and P = 0.02 for III versus I.

reperfusion and inhospital cardiac mortality. As possible univariate predictors, all variables presented in Table I (for noninvasive or invasive indices of reperfusion) or Tables I and II (for inhospital cardiac death) were evaluated, and those with a P value <.1 were introduced in the multivariate models.

Survival curves were analyzed by use of the Kaplan-Meier method, and the log-rank test was used for comparison among curves. Univariate Cox regression analysis, for each variable presented in Tables I and II, was used as a means of determining univariate predictors of long-term cardiac mortal-

Table III. Multivariate* predictors of noninvasive and invasive indices of reperfusion

	Complete ST resolution	P	TIMI 3 flow	P	LVEF <45%	P
Diabetes mellitus					2.55 (1.33-4.92)	.005
History of SA			0.85 (0.66-0.94)	.01		
History of MI					3.19 (1.32-7.74)	.01
Anterior STEMI†	0.77 (0.56-0.90)	.01			6.16 (3.49-10.87)	<.001
Time to thrombolysis	0.89 (0.81-0.92)	.007	0.75 (0.67-0.85)	<.001	1.71 (1.56-1.84)	<.001
Tertiles of CRP						
II vs I	0.70 (0.40-1.23)	.22	0.89 (0.56-1.01)	.06	1.21 (0.68-1.99)	.51
III vs II	0.43 (0.24-0.77)	.004	0.46 (0.23-0.93)	.03	2.24 (1.16-4.32)	.02
III vs I	0.30 (0.17-0.54)	<.001	0.20 (0.10-0.39)	<.001	2.99 (1.44-6.20)	.001

Values presented as relative risk with 95% CI in parentheses. *SA,* Stable angina.
*Univariate predictors are not presented.
†Current event.

ity. Subsequently, all variables with a P value <.1 were included as covariates in a Cox hazard regression multivariate model as a means of identifying independent predictors of long-term cardiac mortality.

All tests were 2-tailed and a P value <.05 was considered to be significant. Statistical analysis was performed with SPSS software (release 10.0, SPSS, Chicago, Ill).

Results

Nine of the 339 patients who were initially recruited were excluded because of premature discontinuation of thrombolysis because of stroke (2), allergic reaction (1), severe bleeding (1), cardiogenic shock and referral for rescue percutaneous coronary intervention (2), or electromechanical dissociation–death (3). Additionally, 11 patients were excluded because of technical problems in electrocardiogram interpretation. Thus, 319 patients comprised the study cohort.

Baseline characteristics

The mean age of the 319 study patients was 60 ± 11 years (range 32-76 years). There were 235 men (73.7%). CRP values ranged from 0.5 to 9.64 mg/dL (median 0.8 mg/dL, 25th and 75th percentiles 0.5 mg/dL and 2.27 mg/dL, respectively). Patients' mean prehospital delay was 4.0 ± 2.9 hours (range, 0.5-12 hours), and no difference was observed among the groups (3.9 ± 2.7, 4.0 ± 3.0, and 3.9 ± 2.9 hours for the first, second and third tertile, respectively, P = .81). The mean creatin kinase-MB level on admission was 40.6 ± 19.3 IU/lt (upper normal limit 17 IU/L). There was no significant relation between CRP levels on admission and either prehospital delay (Spearman's r = 0.05, P = .36) or creatin kinase-MB levels on admission (Spearman's r = 0.19, P = .54), and subsequently, the possibility that high CRP levels on admission had been induced from larger preceding myocardial necrosis seems unlikely.

The mean interval from main pain invasion through thrombolysis initiation was 4.4 ± 2.8 hours (range 0.7-12.5 hours).

One hundred eighty-one patients (56.7%) sustained an anterior STEMI. There was no significant difference in the CRP values between patients with or without an anterior MI (median 0.81 mg/dL vs 0.75 mg/dL, respectively, P = .4).

Differences among tertiles in baseline characteristics are presented in Table I.

Complete ST-segment resolution and CRP tertiles

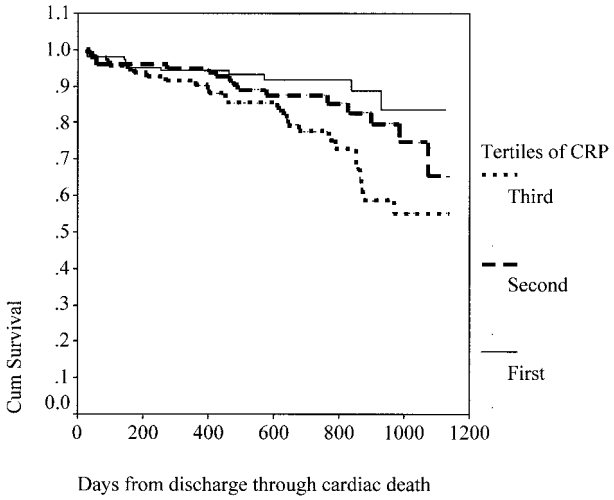
One hundred fifty-five patients (48.6%) had complete ST-segment resolution. The Cohen kappa for interobserver agreement for the presence of complete ST-segment resolution was κ = 0.93, with a 95% CI of 0.89-1.00.

Tertiles of CRP were associated with this noninvasive index of myocardial reperfusion by means of univariate analysis (Table II). In particular, there was a significant gradual decrease in the chance of complete ST-segment resolution with an increase of CRP tertiles. Differences were more profound between the top tertile and the other 2 tertiles. By means of univariate logistic regression analysis, several factors were correlated to the incidence of complete ST-segment resolution (data not presented). CRP tertiles were revealed by means of multivariate logistic regression analysis to be independently related to complete ST-segment resolution (Table III).

TIMI 3 flow, LVEF, and CRP tertiles

Nine patients died before inhospital coronary arteriography, whereas 270 patients (84.6%) underwent coronary arteriography during hospitalization (mean 4.6 ± 1.3, range 1-7 days). There was no significant difference for the interval from admission through inhospital angiography among the 3 groups (Table II).

Figure 1



Kaplan-Meier curves represent postdischarge cumulative survival probability among the tertiles of CRP during the follow-up.

Multivessel coronary artery disease was observed in 75.6% of patients (204/270). The rate of TIMI 3 flow in the infarction-related artery was 60.4%. The mean value of LVEF was 41.4 ± 8.5, and 52.6% of patients (142/270) had an LVEF <45%. The Cohen kappas for interobserver agreement for the TIMI 3 flow and LVEF <45% were $\kappa = 0.90$, with a 95% CI of 0.87-0.99, and $\kappa = 0.92$, with a 95% CI of 0.88-1.00, respectively.

Tertiles of CRP were positively associated with reduced incidence of TIMI 3 flow and decreased LVEF by means of either univariate (Table II) or multivariate (Table III) analysis.

Inhospital and long-term cardiac mortality

Seventeen patients (5.3%) died before discharge. The inhospital cardiac mortality rate was 1.8% (2/110), 3.9% (4/103), and 10.4% (11/106) in first, second, and third tertiles, respectively (Pearson χ^2 0.83 for second vs first, $P = .36$, 3.31 for third vs second, $P = .07$, 7.0 for third vs first, $P = .008$). By means of multivariate logistic regression analysis, CRP tertiles were independently associated with inhospital cardiac mortality (RR [95% CI], 1.78 [0.39-6.17] for second vs first, $P = .59$, 2.87 [0.88-9.31] for third vs second, $P = .08$, 6.24 [1.35-28.83] for third vs first, $P = .02$).

The study patients were observed for a mean period of 22 ± 9 months (range 1-37 months) after discharge. Five patients were lost to follow-up. From the time of hospital discharge through the end of follow-up, 52 patients (52/297, 17.5%) died because of cardiac reasons, and 4 patients (4/297, 1.3%) died because of noncardiac reasons (cardiac death 9.5% [10/105], 16.3% [16/98], and 27.7% [26/94], non-cardiac death 0.9% [1/105], 0.0% [0/98] and 3.1% [3/94] in the first, second, and third tertiles, respectively). Kaplan-Meier curves showed that patients in the top tertile had a statistically significant decreased probability of long-term cardiac survival compared with other patients, especially those in the bottom tertiles (log rank χ^2 1.39 for second vs first, $P = .24$, 3.76 for third vs second, $P = .05$, 9.1 for third vs first, $P = .002$) (Figure 1).

By means of univariate Cox regression analysis, tertiles of CRP and several other variables were found to be related to long-term cardiac mortality (Table IV). However, by means of the multivariate stepwise Cox hazard regression model, only diabetes mellitus and CRP tertiles were positively related to long-term cardiac mortality, whereas LVEF was negatively associated with long-term cardiac mortality (Table IV).

Discussion

The primary finding of this study is that elevated plasma CRP levels on hospital admission in patients with STEMI are strongly associated with thrombolysis failure and with more ominous short- and long-term prognoses. Although many prospective studies have been conducted to evaluate the role of CRP in the prognosis of patients with stable or unstable coronary syndromes,[19] there is a lack of data about a possible association of plasma CRP levels on admission with response to thrombolysis.

In this study, tertiles of CRP were found to be significantly associated with the incidence of complete ST-segment resolution and, during hospitalization, estimated TIMI 3 flow in the infarction-related artery or the LVEF. Moreover, CRP tertiles were positively related to either the inhospital or long-term cardiac mortality rate. The aforementioned associations were constantly significant by means of both univariate and multivariate analysis, and, thus, the possibility of their emerging by chance is considered to be unlikely.

The possible relationship of plasma CRP levels with short- and long-term prognosis in patients with acute MI has been investigated and a positive association has been reported in all the studies. Gheno et al,[20] who studied 205 consecutive elderly women without thrombolysis, have reported that a high plasma CRP on admission was independently and positively related to inhospital mortality. Tomoda et al[21] have found that elevated CRP levels in the first 6 hours of acute MI were positively associated with more inhospital adverse outcome, including cardiac death after primary percutaneous coronary intervention. Nikfardjam et al,[22] in a cohort of 729 patients with acute MI, have retrospectively shown that there was a positive associ-

Table IV. Univariate and multivariate predictors of long-term cardiac mortality

	Univariate Cox analysis	P	Multivariate Cox analysis	P
Age (y)	1.03 (0.99-1.05)	.06		
Males	0.52 (0.30-0.91)	.02		
Diabetes mellitus	3.89 (2.26-6.71)	<.001	3.17 (1.81-5.53)	<.001
History of MI	1.67 (0.83-3.32)	.15		
Time from onset of pain to thrombolysis administration in hours	1.10 (0.99-1.18)	.06		
Anterior STEMI*	2.51 (1.36-4.64)	.003		
Tertiles of CRP				
II vs I	1.60 (0.73-3.54)	.24	1.53 (0.64-3.44)	.49
III vs II	1.84 (0.98-3.43)	.05	1.67 (0.92-3.78)	.07
III vs I	2.92 (1.41-6.05)	.004	3.22 (1.50-6.93)	.01
Complete ST resolution	0.23 (0.11-0.45)	<.001		
TIMI 3 flow	0.31 (0.17-0.55)	<.001		
LVEF <45%	6.43 (3.08-13.41)	<.001	4.99 (2.14-8.57)	<.001

Values presented as hazard ratio with 95% CI in parentheses.
*Current event.

ation between plasma CRP levels on admission and 3-year cardiac mortality. Tommasi et al[23] have shown that patients with increased levels of CRP early in the first 8 hours of uncomplicated MI constituted a high-risk group for the composite end point of cardiac death and new acute coronary events during the first year. Pietilä et al[14] have demonstrated a gradual inverse relationship between peak plasma levels of CRP, estimated during the first days of STEMI, and the 24-month survival probability. However, in Pietilä's study, CRP measurements were made late in the course of MI, and subsequently, CRP values were significantly influenced by the extent of intercurrent myocardial necrosis. In this study, blood sampling was done early, and, therefore, there were not significant differences in CRP values between anterior and nonanterior MI and there was no relationship between CRP and either prehospital delay or creatin kinase-MB levels on admission. However, the possibility that elevated plasma CRP levels constitute an epiphenomenon could not be definitely excluded. Larger myocardial necrosis or longer prehospital delay may be associated with both elevated plasma CRP levels and with less likelihood of successful reperfusion and worse outcome.

This study implies a possible role of inflammation in the pathophysiologic mechanisms underlying response to thrombolysis and short- and long-term cardiac mortality in patients with STEMI. Increased inflammatory response in the coronary atherosclerotic plaques, coronary vasculature, or myocardial cells may be involved. Increased cytokine release, by local inflammatory cells, circulating inflammatory cells, or both, may activate vascular endothelium, resulting in the attenuation of its antiplatelet, antithrombotic, or vasorelaxating properties.[24] This endothelial dysfunction may account for thrombolysis failure and increased short- and long-term mortality in patients with elevated plasma CRP levels.

In this study, LVEF was negatively related to long-term cardiac mortality, whereas the presence of diabetes mellitus was associated with a >2-fold increase in the risk of cardiac death after hospital discharge. Numerous randomized thrombolytic trials have established the strong and independent adverse influence of postinfarction low LVEF on long-term cardiac survival.[5] Additionally, it is well-known that patients with diabetes mellitus and STEMI are at a higher risk for future fatal or nonfatal cardiovascular events, even after the administration of thrombolysis.[25,26]

Clinical implications

Our results have demonstrated that a high CRP value before the start of intravenous thrombolysis is strongly associated with reperfusion failure, as measured by means of ST-segment resolution, TIMI 3 flow, or LVEF and short- and long-term cardiac mortality. The additional information derived from CRP measurements was independent of the other studied clinical variables, with possible influence in risk stratification and treatment of patients with STEMI. Patients with elevated CRP levels on admission may need special attention for the identification of thrombolysis failure and possibly the appropriate adjustment of treatment.

Limitations of the study

Although this prospective study was specifically designed to address the possible association of CRP measured early in the course of STEMI, with thrombolysis effectiveness and cardiac mortality, there was no random allocation of the several therapies in our cohort. However, baseline CRP values were decoded at the

end of the study and, therefore, a bias was not introduced by these measurements in the treatment of the studied patients.

The recently recommended high sensitivity CRP assay was not used because it was not available at the time the study was designed.

The study patients had not undergone catheterization immediately after the administration of intravenous thrombolysis. Therefore, the estimated TIMI grades do not represent the flow in the infarction-related artery early after thrombolysis administration. However, complete ST-segment resolution is a reliable predictor of myocardial reperfusion and is well related to TIMI 3 flow in the infarction-related artery after thrombolysis.[27,28]

Permanent ST-segment elevation and impaired TIMI flow in the infarction-related artery may accompany past MI. Therefore, our results might have been influenced by the inclusion of such patients. However, no significant differences were observed for the prevalence of past MI among the CRP tertiles.

The low rate of rescue percutaneous coronary intervention in our institute and the small cohort size should be taken into account in the interpretation or possible generalization of our results.

Finally, the predictive value of the several variables introduced in the multivariate Cox regression model might have been altered if LVEF had been estimated after the dissolution of the acute phase myocardial stunning and by means of a more appropriate method (radionuclide angiography). However, the accumulative evidence of the independent predictive value of CRP on the long-term cardiac mortality in a large spectrum of patients with coronary artery disease or in healthy individuals[19] and the high statistical significance of our results make these associations specifically possible.

Conclusions

High plasma levels of CRP on admission in patients with STEMI may be positively associated with inadequate response to intravenous thrombolysis and unfavorable short- and long-term prognosis. If these results can be validated by other larger, multicenter, specifically-designed prospective studies, risk stratification and treatment of patients with STEMI may improve.

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Increased myocardial ischemia after food is not explained by endothelial dysfunction

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Background Recent studies suggest that a high-fat meal can impair endothelial function. The aim of this study was to determine whether greater myocardial ischemia after either a low-fat or a high-fat meal is associated with an increase in brachial artery endothelial dysfunction.

Methods Twenty subjects with coronary artery disease and ≥1-mm ST-segment depression during exercise were studied. In a randomized, double-blind, crossover design, ST-segment changes during treadmill exercise and brachial artery diameter and flow-mediated dilation were measured before and 3 hours after a low-fat milkshake meal or the same meal supplemented with 64 grams of cooked fat.

Results After the low-fat but not the high-fat meal, resting brachial artery diameter decreased (before meal 4.72 ±0.50 mm, after low fat meal 4.62 ±0.49 mm, $P = .001$; after high fat meal 4.70 ±0.51 mm, not significant). High-flow brachial artery diameter was similar before (4.81 ± 0.48 mm) and after the low-fat (4.82 ± 0.48 mm) and high-fat (4.84 ± 0.48 mm) meals ($P > .05$ for all). Brachial artery flow-mediated dilation was not impaired after either meal. Exercise duration decreased more after the low-fat meal (mean change 39 seconds, 95% CI −14 to −63 seconds, $P = .004$) than after the high-fat meal (−7 seconds, 95% CI +19 to −34 seconds, not significant). ST-segment depression during equivalent exercise was greater after compared with before both meals (before meals 1.03 ± 0.69 mm, after low fat 1.27 ± 0.80 mm, $P = .03$; after high fat 1.24 ± 0.74 mm, $P = .04$).

Conclusions Increased myocardial ischemia after food is caused by mechanisms other than endothelial dysfunction and by meal components other than cooked fat. (Am Heart J 2002;144:e8.)

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