C-Reactive protein in acute myocardial infarction: Association with heart failure

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Background High C-reactive protein (CRP) levels have been associated with higher mortality rate in patients with acute myocardial infarction (AMI). However, it is not known whether inflammation plays a role in the time-course of heart failure (HF) in this clinical setting. Our aim was to study the nature of the relationship between CRP and HF during AMI.

Methods This prospective study was carried out in 269 subjects admitted to the hospital for suspected AMI. Of these, 220 had evidence of AMI. The other 49 subjects were studied as controls. CRP was assessed on the first, third, and seventh day after admission.

Results CRP was significantly higher in the patients with AMI than in the control patients ($P = .001$) and peaked on the third day. Among the patients with AMI, CRP was higher in patients with HF than in patients without HF (adjusted $P = .008$, $P = .02$ and $P = .03$ on 1st, 3rd, and 7th day, respectively). Prevalence of HF on admission was slightly higher in the subjects with first-day CRP ≥15 mg/L than in those with CRP <15 mg/L, and the between-group difference progressively increased from the first to the seventh day ($P < .0001$). At multivariable regression analysis, first-day log-CRP was shown to be a strong independent predictor of both HF progression ($P < .0001$) and left ventricular ejection fraction ($P < .0001$). One-year total mortality and HF-mortality rates turned out to be higher in the patients with CRP ≥85 mg/L than in those with CRP below that level ($P < .0001$), and log–third-day CRP was independently associated with 1-year mortality at multivariable analysis ($P = .0001$).

Conclusions CRP on admission to hospital is suitable for predicting the time-course of HF in patients with AMI. Peak CRP value is a strong independent predictor of global and HF-mortality during the following year. (Am Heart J 2003;145:1094-101.)

Accumulated data suggest that markers of acute inflammation such as C-reactive protein (CRP) may be reliable predictors of outcome in patients with ischemic heart disease.[1-3] Although the prognostic value of CRP in patients with myocardial infarction has not been tested in large studies, several data indicate that CRP is an important marker of risk also in this clinical setting.[4-6] The high incidence of heart failure (HF) during acute myocardial infarction (AMI) and the strong influence of HF on mortality make it one of the most challenging problems to deal with in this clinical setting.[7,8] Older age, extension of necrosis area, previous AMI, diabetes mellitus, hypertension, and anterior site of AMI are considered among the most important features leading to HF during AMI.[9-12] In a 2-year follow-up of 188 patients with AMI, Pietila et al[13] observed that the subjects who died of congestive HF had elevated CRP levels. On the other hand, increased plasma levels and myocardial expression of inflammatory mediators occur in experimental and clinical HF,[14,15] suggesting that inflammation can play a key role in the pathogenesis of congestive HF.

To the best of our knowledge, no study reported on whether there is a relationship between CRP and HF during the acute phase of myocardial infarction. The aim of this study was to test the hypothesis that there is a relationship between high CRP levels and HF progression during the first week of hospitalization for AMI, and that high CRP level is associated with HF-related death and global mortality after AMI.

Methods

Patients

Three hundred and five unselected and consecutive patients admitted to 2 intensive-care units in 2 urban general hospitals for suspected AMI were prospectively studied. Thirty-three patients with preexisting or acute inflammatory pro-

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cess, neoplastic disease, or incomplete data collection, and 3 patients who died within 3 days after admission were excluded. Thus, the final analysis was performed in 269 subjects.

The patients were interviewed by a physician who completed a standard record form covering details of medical history. All patients gave their informed consent and the study was approved by the hospitals' ethics committees.

Measurements

All clinical and laboratory data were obtained during the first week of hospitalization. In 39 patients, seventh-day data were not available because of early discharge or death.

The criteria for AMI diagnosis were based on fulfillment of at least 2 of the following: central chest pain lasting >30 minutes, typical changes in serum enzymes (total creatine kinase [CK], CK-MB, aspartate aminotransferase, lactate dehydrogenase), typical electrocardiogram changes with occurrence of pathological Q waves and/or localized ST-T changes in at least 2 contiguous leads.[16]

Upon admission and thereafter every 4 hours, serum enzymes dosage and 12-lead electrocardiogram were carried out. Starting from the third day of admission, the above exams were performed daily. On the first and seventh days after admission, venous blood was drawn for determination of standard biochemistry. The inhospital length of bed rest was similar for patients with AMI and controls during the 7 days of the study.

CRP measurement

In all patients, venous blood was drawn on the first, third, and seventh days for measurement of CRP. In the whole sample, CRP on the first day was measured 13.30 (1.00-23.15, median [5th 95th percentile]) hours after admission, and 19.00 (3.50-56.15) hours after onset of symptoms. Venous blood samples were put in ice and centrifuged within 20 minutes at 4°C, and the plasma was stored at −20°C until assayed (storage time <1 month). CRP was measured at the University of Padova by means of the nephelometric method with particle-bound goat antihuman CRP (Beckman Instruments, Inc, Fullerton, Calif) and expressed as mg/L. The lower limit of the measurements range of the assay was 1 mg/L.[17]

HF evaluation

The presence and degree of HF was assessed on the first, third, and seventh days after admission following the Killip classification.[18] To describe the progression of HF during the first 7 days of hospitalization, subjects were divided into 4 classes: class 1, Killip class 1 in all examinations; class 2, Killip class >1 at entry and then improving to Killip class 1 within the seventh day; class 3, Killip class 1 on admission and then worsening to Killip class >1 in the following days; class 4, Killip class >1 in all examinations. This variable will be called "HF-progression class" (1-4) throughout the paper.

To evaluate left ventricular ejection fraction (LVEF), a 2-dimensional echocardiogram was performed in 207 patients with AMI between the third and the seventh day after admission. Determination of LVEF (%) was performed according to Simson's method.[19] Sixteen patients in whom the echocardiographic images were technically unsatisfactory were discarded from the analysis. Thus, LVEF could be obtained for 191 patients. Hormones reflecting HF were assessed on the first, third, and seventh day after admission: plasma renin was measured by immunoradiometric assay and aldosterone by radioimmunoassay, using kits from Nichols Institute (San Juan Capistrano, Calif), and Radim, Angleur (Liège, Belgium), respectively.

Follow-up

One year after recruitment each patient was called for a clinical check-up. For those who died during a hospital stay, date and cause of death were obtained from hospital records (including postmortem report where available). Mortality data for those who died outside the hospital were obtained from the family doctor. No patient dropped out during follow-up. End points used for the present study were global mortality and HF mortality.

Statistical analysis

Statistical analysis was made using Systat 7.0 for Windows package (SPSS Inc, Evanston, Ill) and JMP 4.0 for Windows (SAS Institute Inc, Cary, NC). Data accrued on each patient included both measured (continuous) and categorical variables. Skewed variables were log-transformed before analysis. Killip class was considered a 4-class variable. Continuous variables were utilized either in the "native state" or a dichotomous variable by means of a cut off point assessed using ROC curves analysis (MedCalc, Ver. 4.16H, Win 95, 1993-97, NL).

Comparisons between groups were made by the Student *t* test or ANCOVA and an overall between group repeated measure ANCOVA with Tukey post-hoc tests, wherein data from all 3 days of observation were simultaneously assessed for continuous variables. The covariates used in each comparison are reported in the Results section. The Pearson χ^2 test and the Fisher exact test were used for categorical variables.

Survival analysis was first performed entering variables in their "native state" (continuous, ordinal, or nominal) in the Cox models, then as dichotomous variables in the assessment of risk ratios.[20]

Survival curves based on dichotomized CRP levels were constructed by the Kaplan-Meier method and compared by log-rank test. Further, the risk ratios of the univariate and multivariate analyses and corresponding 2-sided 95% CIs were derived from the regression coefficients in the Cox models.

Finally, analyses to discern association between HF and other clinical variables were investigated. Variables significantly associated with HF and LVEF by these univariate analyses and those known to be of clinical relevance were entered as independent variables in a logistic regression analysis with HF-progression class (classes 1 and 2 vs classes 3 and 4) as the dependent variable, and a multiple regression analysis (using the General Linear Model) with LVEF as the dependent variable (minimum tolerance for entry into models = 0.01). For all multivariable regressions, a final parsimonious model was performed and the results are reported in Tables I and II.

Data are presented as mean ± SD for continuous measures unless otherwise specified and as proportion of patients with a characteristic for categorical variables. All *P* values are 2-tailed and statistical significance was established as $P < .05$.

Table I. Independent predictors of heart failure (logistic regression analysis) and of left ventricular ejection fraction (linear regression analysis)

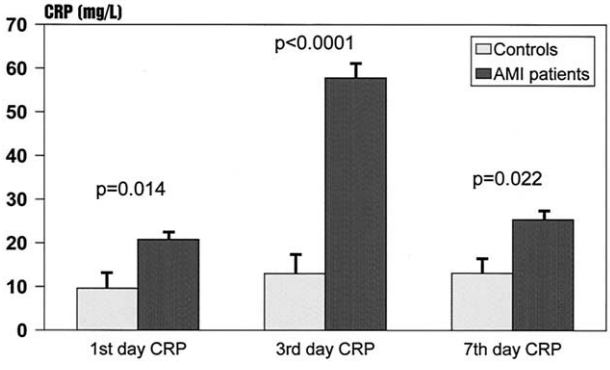
	HF-progression class		LVEF%	
Independent variables	**T**	***P***	**T**	***P***
C-reactive protein	4.3	<.0001	−3.9	<.0001
Age	3.3	<.0001	−3.9	<.0001
Anterior site of myocardial infarction	3.0	.002	−4.5	<.0001
Aldosterone	2.1	.03		
Previous myocardial infarction			−6.3	<.0001
CK-peak			−3.0	.003

Initial models included age, sex, body mass index, log–CK-peak, hypertension, diabetes, history of angina, history of myocardial infarction, anterior site of myocardial infarction, thrombolytic therapy, 1st day renin, 1st day aldosterone, log-1st day C-reactive protein. Final models included only the above reported variables. *HF*, Heart failure; *LVEF*, left ventricular ejection fraction.

Table II. Univariate and final multivariable Cox proportional hazards models for 1-year all-cause mortality in the patients with acute myocardial infarction using all variables in their "native state".

	Univariate			Multivariable		
Independent variables	**Regression coefficient ± SE**	**χ^2 value**	***P***	**Regression coefficient ± SE**	**χ^2 value**	***P***
Age	0.09 ± 0.02	30.9	<.0001	0.07 ± 0.02	12.6	.0004
Log-C-reactive protein	0.83 ± 0.18	28.4	<.0001	0.56 ± 0.16	15.5	.0001
Killip class	1.58 ± 0.21	39.4	<.0001	0.99 ± 0.23	15.4	.0001
Thrombolysis	−1.57 ± 0.42	18.7	<.0001	−0.90 ± 0.43	5.0	.02

Figure 1



CRP measured on the first, third, and seventh day after admission to hospital in 220 patients with acute myocardial infarction and 49 control subjects (ANCOVA for repeated measure, $P = .001$). Values are means and *error bars* indicate SEM.

Results

Of the 269 patients included in the study, 220 had evidence of AMI on the basis of the aforementioned criteria. The other 49 subjects were used as a control group. Of these, 32 manifested signs of unstable angina, 10 had chronic ischemic heart disease, and 7 had nonischemic diseases. The 2 groups were balanced for age and sex. Nitrates, antiplatelets, and anticoagulants were more frequently used in the patients with AMI ($P = .006$, $P = .008$ and $P < .0001$, respectively), and calcium-channel blockers in the controls ($P < .0001$).

CRP in patients with AMI and controls

CRP was significantly higher in the patients with AMI than the control group (repeated measure adjusted $P = .001$) (Figure 1). The Tukey test showed that the between-group differences were significant on all 3 days of measurement. In the AMI group, 7 (3.2%) patients were taking statins before admission and 42 patients (19.1%) started statin treatment during the first week of hospitalization. CRP levels were similar in the patients with or without statin treatment (repeated measure age adjusted $P = .16$). Also, CRP trend during the week of hospitalization did not differ between the 2 subgroups ($P = .47$ for trend).

CRP and HF

Among the patients with AMI, 86 (39%) showed clinical signs of HF (Killip class >1) during the week of

Table III. Clinical characteristics of the patients with acute myocardial infarction divided by absence or presence of heart failure during the first week of hospitalization.

	No HF (n = 134)	HF (n = 86)	P
Age (y)	64.1 ± 10.9	70.7 ± 10.9	<.0001
Sex (females)	23 (17)	34 (39)	<.0001
Body mass index (kg/m^2)	26.9 ± 3.6	26.5 ± 4.6	ns
Previous myocardial infarction	15 (11)	21 (24)	.01
History of angina	15 (11)	15 (17)	ns
Current smoking	59 (44)	23 (27)	.01
Hypertension	63 (47)	41 (48)	ns
Diabetes mellitus	23 (17)	34 (39)	<.0001
Systolic blood pressure (mm Hg)	124 ± 21	121 ± 19	ns
Diastolic blood pressure (mm Hg)	75 ± 11	73 ± 11	ns
Heart rate (beats/min)	69 ± 12	77 ± 15	<.0001
Time to CCU (hours)*	3.00 (1.05-13.00)	3.00 (1.15-20.20)	ns
CK peak (UI/L)	1583 ± 1377	1994 ± 1711	ns
CK-MB peak (UI/L)	174 ± 140	216 ± 187	ns
Total cholesterol (mg/dL)	214 ± 41	202 ± 46	ns
HDL-cholesterol (mg/dL)	46 ± 12	47 ± 11	ns
Triglycerides (mg/dL)	154 ± 88	138 ± 77	ns
LVEF(%) (n = 191)	54 ± 10	40 ± 13	<.0001
Thrombolysis	67 (50)	38 (44)	ns
Nitrates	133 (99)	82 (95)	.05
β-Blockers	81 (60)	27 (31)	<.0001
Calcium-channel blockers	17 (13)	11 (13)	ns
Diuretics	18 (13)	63 (73)	<.0001
ACE-inhibitors	31 (23)	51 (59)	<.0001
Digitalis	2 (1)	23 (27)	<.0001
Antiarrhythmics	14 (10)	29 (34)	<.0001
Antiplatelets	129 (96)	82 (95)	ns
Anticoagulants	134 (100)	85 (99)	ns

Values presented as mean ± SD or number (percent) unless otherwise indicated. *CK-MB*, Creatin kinase-MB isoenzyme; *ns*, not significant.
*Time from onset of symptoms to arrival at coronary care unit; median (5th-95th percentile).

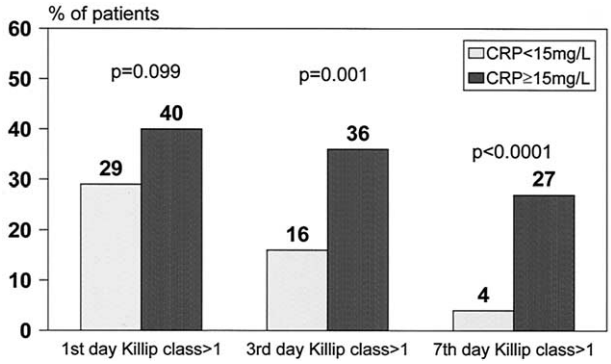
study (Table III). Patients with HF were older, more frequently were female and had diabetes, and had a higher heart rate and a smaller LVEF than patients without HF. Time to presentation from onset of symptoms to coronary care unit, and peak CK-MB did not differ between the 2 groups.

Because the present analysis focuses on prediction of CRP for HF progression during the first week of hospitalization, chiefly first-day and third-day CRP data were considered for the analyses. First-day CRP was higher among patients with HF than patients without HF (30 ± 4 vs 15 ± 3 mg/L [adjusted for confounders reported in Table III, $P = .008$]). Also, third-day and seventh-day CRP values were higher among patients with HF (73 ± 7 vs 48 ± 5 mg/L, adjusted $P = .02$ and 34 ± 4 vs 20 ± 3 mg/L, adjusted $P = .03$, respectively).

According to ROC curve analysis, the first-day CRP cut-off value that best identified the patients prone to HF progression approximated 15 mg/L. Prevalence of HF on admission was slightly higher in the subjects with first-day CRP ≥15 mg/L compared with those with first-day CRP <15 mg/L. However, the between-group difference in the prevalence of HF progressively increased from the first to the seventh day after admission (Figure 2). After 1 week, only 4% of the patients with first-day CRP <15 mg/L were still in Killip class >1, while among the patients with CRP ≥15 mg/L, 27% were in Killip class >1. Accordingly, LVEF was higher in the former than in the latter (51% ± 12% and 44% ± 14%, respectively, adjusted $P < .0001$).

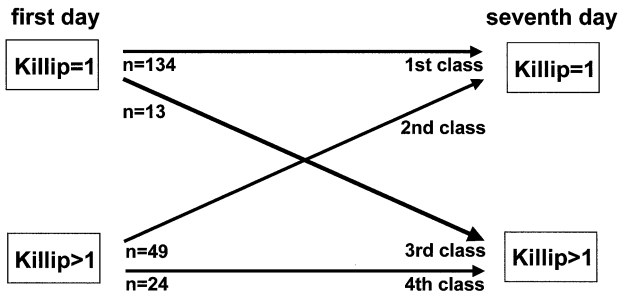
In the patients divided by HF-progression score (class 1-4), first-day and third-day CRP values resulted lower in HF-progression classes 1 and 2, than in classes 3 and 4 (adjusted $P < .0001$ for both first- and third-day data) (Figure 3), irrespective of whether they received thrombolytic agents. Thus, CRP values were low not only in patients without HF during the whole week (HF-progression class 1) but also in those with HF on admission who passed to Killip class 1 during the subsequent days (HF-progression class 2). Conversely, high first-day and third-day CRP levels were found not only in patients with persistent HF (HF-progression class 4) but also in those who passed from Killip class 1 to Killip classes >1 within the week of observation (HF-progression class 3).

Figure 2



Prevalence of HF on the first, third and seventh day after admission in patients divided by CRP levels ≥15 mg/dL or <15 mg/L measured on the first day.

Figure 3



HF-progression class	1st day CRP
1st	15±3
2nd	15±5
3rd	41±9
4th	56±6

Time-course of HF during the week of hospital stay and CRP measured on the first day of hospitalization in 220 patients with AMI divided into 4 classes of HF progression during the week following admission to hospital (see Methods for explanation).

Predictors of heart failure

To verify whether first-day CRP was independently associated with heart decompensation during the week of study, a number of multivariable regression analyses were made, considering 13 variables (Table I) significant at univariate level. In a first model (logistic), HF-progression score was used as dependent variable (classes 1 and 2 vs classes 3 and 4), while in a second one (linear), the dependent variable was echocardiographic LVEF (Table I). In the final parsimonious models, first-day CRP was independently associated with HF indicators in both models. Age, peak CK, previous AMI, anterior site of AMI, and aldosterone were other independent predictors of HF. When statin treatment (as dicotomic variable) was included in the models, results remained virtually unchanged. Third-day CRP was still a significant predictor of HF progression and LVEF, but to a lower level of statistical significance (T = 2.5, $P = .01$; T = 2.6, $P = .01$, respectively). No association was found between seventh-day CRP and HF-progression score. In addition, we divided the patients with AMI into 2 subgroups according to peak CK values (above or below the median in the group). At multivariable analysis (using the parsimonious model of Table I), prediction of CRP for HF-progression was significant both in the high peak-CK subgroup (T = 3.2, $P = .001$) and in the low peak-CK subgroup (T = 2.9, $P = .004$).

In order to further ascertain whether the association between CRP and HF was independent from extension of necrosis, the 74 patients with first-day CRP above the 15 mg/L cut-off (mean 51 ± 5 mg/L) were matched with 74 patients with CRP below that value (mean 6 ± 0.3 mg/L) and with the same peak CK-MB (mean values 204 ± 177 and 196 ± 159 UI/L, respectively, $P = .88$). Age and sex were well balanced in the 2 groups. On the first day, prevalence of HF was 40% in the high-level-CRP group and 31% in the low-level-CRP group (P = not significant), on the third day it was 36% and 16%, respectively ($P = .005$), and on the seventh day it was 27% and 4%, respectively ($P < .0001$). Within the high-level-CRP group, the patients with HF-progression score >2 were 34%, whereas within the low-level-CRP group, those with HF-progression score >2 were 5% ($P < .0001$). LVEF was 43% ± 15% in the former and 51% ± 12% in the latter ($P = .002$). Matching the patients by peak CK instead of peak CK-MB (mean values 1875 ± 1533 IU/L and 1924 ± 1659 IU/L, $P = .95$) gave virtually identical results.

One-year mortality

During the year of follow-up, 40 (18%) patients (28 men and 12 women) died. Twelve died of HF or cardiogenic shock. Other causes of death were reinfarction in 3 subjects, stroke in 3, sudden death in 10, other cardiovascular causes in 11, and noncardiovascular causes in 1. Twenty-one (9%) subjects underwent PTCA and 18 (8%) underwent CABG during the year of follow-up.

Because the relation with mortality was stronger for third-day CRP (peak value), only data for this value are provided. According to ROC curve analysis, the third-day CRP cut-off value that best discriminated between the patients prone to death and survivors approximated 85 mg/L. By dividing the 40 patients who died according to whether they had CRP ≥85 mg/L or <85

mg/L, all-cause mortality rate turned out to be higher ($P < .0001$) in those with CRP ≥85 mg/L (Table IV). Moreover, death from HF was much more common in the patients with high CRP (18%) than in those with low CRP (1%) ($P < .0001$).

Kaplan-Meier curves related to third-day CRP are shown in Figure 4. Mortality rate was much higher in the subjects with CRP ≥85 mg/L than in those with CRP <85 mg/L (log-rank test $\chi^2 = 51.7$, $P < .0001$).

At univariate Cox analysis, CRP was associated with global mortality rate (Table II). In a multivariable final parsimonious Cox proportional hazards regression analysis including age, Killip class, and thrombolysis (in a negative fashion), which were all significant at univariate level, CRP remained strongly associated with global mortality (Table II). When the same analysis was repeated in the subset of subjects with echocardiographic LVEF (n = 191), CRP remained a strong correlate of mortality ($\chi^2 = 15.3$, $P = .0001$).

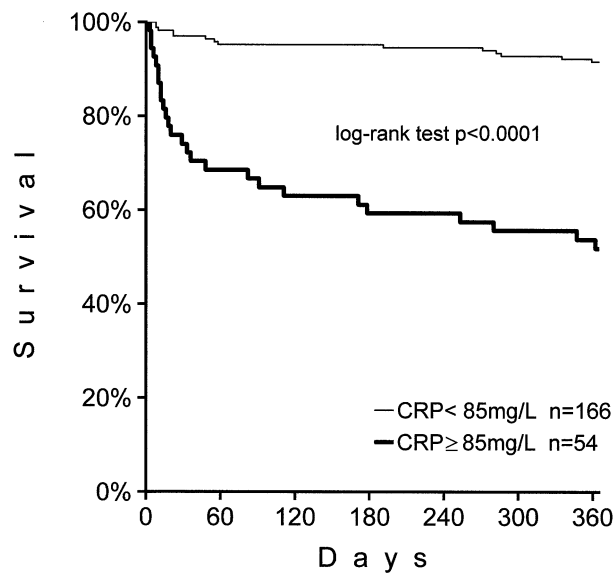
Relative risk (RR) for all-cause mortality for CRP values ≥85 mg/L was 7.6 (confidence limit 4.0-15.0). RR remained elevated also after adjustment for the variables considered in the Cox model (5.5, 2.8-11.0), and additional adjustment for LVEF confirmed the independent association of CRP with mortality (RR 5.7, confidence limit 2.7-12.2).

Table IV. One-year mortality rate in the patients divided according to C-reactive protein measured on the third day after admission to hospital.

	CRP <85 (n = 166)	CRP ≥85 (n = 54)	χ^2	P
Global-mortality rate (%)	14 (8)	26 (48)	43.2	<.0001
HF-mortality rate (%)	2 (1)	10 (18)	23.7	<.0001
Other cardiovascular causes (%)	12 (7)	16 (30)	18.4	<.0001

CRP, C-reactive protein.

Figure 4



Kaplan-Meier estimates of the probability of 1-year all-cause mortality in the patients stratified by CRP ≥85mg/L or <85mg/L measured on the third day after admission ($P < .0001$ for log-rank test).

Discussion

CRP and congestive heart failure

Although several data support the role of inflammatory response in long-term clinical events in AMI,[4-6] data defining the association between baseline CRP elevation and subsequent development of heart failure within this clinical entity is limited. A correlation between peak CRP levels and mortality from heart failure was described in 2 studies performed in small groups.[13,21] To our knowledge, the present study is the first to highlight the relationship between baseline CRP and occurrence of heart failure in the first few days after AMI. Our data showed that CRP soon after admission was higher in patients with AMI with clinical signs of HF compared to those in Killip class 1. Moreover, in the subjects stratified by CRP level at entry (cut-off value 15 mg/L), the difference in the prevalence of HF between the patients with low CRP and those with high CRP progressively increased from the first to the seventh day. Also, patients without signs of HF at entry who developed signs of LV dysfunction in the following days had elevated CRP level on the first day. Conversely, virtually no patient in Killip class 1 with low CRP values at baseline developed signs of HF from the first to the seventh day after admission.

These data suggest that CRP may predict the risk of HF or may play a direct role in augmenting microvascular inflammatory response after ischemic insult.[22] In other words, the marked CRP rise in patients with AMI with HF at entry or in those who developed HF in the subsequent days may not only be an epiphenomenon but may represent a pathogenic process that leads to myocardial damage and left ventricular dysfunction.[22,23] Previous data indicate that CRP may induce complement activation, and a pathogenetic role of complement activation that may lead to maladaptive cardiac remodeling has been described in acute ischemic left ventricular damage.[24,25]

In this report, the time-related association between inflammatory reaction and heart decompensation was studied not only using clinical signs of HF but also LVEF, an objective estimate of LV dysfunction, obtaining parallel results. In agreement with other reports,

peak values of CRP were generally observed on the third day after AMI.[26] However, the relationship between third-day CRP and HF progression was weaker than that for first-day CRP. These data highlight the primacy of the inflammatory process in the observed relationship between CRP and HF. The acute inflammatory reaction in AMI starts 4 to 8 hours after the onset and peaks within 3 to 4 days.[23,26] In this study, first-day CRP was measured 19 hours after onset of symptoms when the acute-phase response was already initiated. Bearing the above in mind, it stands to reason that CRP and the subsequent complement activation may play a pathogenetic role in the development of postinfarction HF.

CRP and prognosis in AMI

Previous studies examining the relationship between CRP and cardiovascular mortality in patients after AMI have found that peak CRP level predicts both inhospital mortality and the long-term outcome.[5,13] The present analysis confirms the prognostic significance of elevated CRP beyond that defined by traditional risk predictors after AMI. The peak CRP cut-off value that best discriminated between the patients prone to death and those who survived was 85 mg/L. In agreement with the results of others, CRP level proved to be a strong predictor chiefly of mortality from HF. In fact, the incidence of death from HF was only 1% among the patients with peak CRP $<$85 mg/L at baseline, while it was 20% among those with peak CRP above that value.

Limitations of the study

Several limitations of our study should be mentioned. We are aware that the cut-off values for CRP prediction of events were based on a statistical test and not on prospective data. Only longitudinal studies in larger groups will confirm the validity of our cutoffs.

We have no data to establish whether thrombolysis was successful or not, and this could affect the incidence of HF and the rate of cardiovascular events, as well as the levels of CK.

Finally, peak CK and peak CK-MB were used as estimates of infarct size, while data on troponin level could have provided a more precise measure of extension of necrosis. However, troponin measurement was not available in our hospitals in 1995 when the study was initiated.

Conclusions

The present results show that CRP on admission to hospital is suitable for predicting the time-course of LV function in patients with AMI. Not only did a CRP value $\geq$15 mg/L identify patients with HF at entry, it also predicted worsening of LV function in patients without clinical signs of HF at entry. Conversely, low first-day CRP values in patients with HF at entry predicted improvement of Killip class in the subsequent days. Furthermore, in agreement with the results by others, peak CRP value was a strong independent predictor of all-cause and HF mortality during the following year. Although the precise role of CRP requires further elucidation, a focus on CRP within the first 3 days after AMI may prove useful for identification of patients who are at greater risk of heart failure and mortality.

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Prospective evaluation comparing the effects of enalapril and losartan in left ventricular remodeling after acute myocardial infarction

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Background

Previous studies have compared angiotensin receptor blockers and angiotensin-converting enzyme inhibitors in patients with heart failure, but there are few data about the effect of these drugs regarding left ventricular remodeling after myocardial infarction.

Methods

Fifty-two consecutive patients with first anterior wall myocardial infarction within 24 hours of evolution were randomized to receive enalapril (as much as 20 mg; mean, 14.6 mg), or losartan (as much as 50 mg; mean, 48 mg). Left ventricular ejection fraction and ventricular volumes were analyzed in 2 serial radionuclide ventriculograpies, carried out within 4 days after the infarction (mean, 97.4 ± 114.2 hours) and after 6 months (mean, 177.7 ± 16.7 days). Ventriculographies were analyzed by a single blinded observer. Mainly because of the unexpected large SD values obtained, the power of the study to demonstrate equivalence between the groups was only 15.7%.

Results

The differences obtained between the first and the second ventriculographies, for the enalapril and losartan groups, were: for left ventricular ejection fraction, −0.4% ± 6.6% versus −1.1% ± 5.9% (P = . 67; 95% CI, 2.77-4.23); for final systolic volume, 0.07 ± 7.7 mL/m^2 versus −0.2 ± 6.1mL/m^2 (P = . 85; 95% CI, −3.57-4.26); for final diastolic volume −0.7 ± 12.1 mL/m^2 versus −3.6 - 9.9 mL/m^2 (P = . 34; 95% CI, −3.22-9.17).

Conclusion

This study, although underpowered, suggests that neither enalapril nor losartan was superior as compared with each other for left ventricular remodeling after myocardial infarction; however, powerful evidence of equivalence was not provided. (Am Heart J 2003;145:e27.)