

C-Reactive Protein in Diabetic and Nondiabetic Patients With Acute Myocardial Infarction

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Atherosclerosis has been reported to be associated with chronic low-grade inflammation of the vascular structure and the endothelial cells (1–4). C-reactive-protein (CRP) is a marker for inflammation and is enhanced in both atherosclerosis and coronary artery disease (5–7). CRP plasma levels above the cutoff of 3 mg/l, as assessed with high-sensitivity immunoassays, have been shown to indicate an increase in cardiovascular risk (8). Diabetes is an independent risk factor of atherosclerosis (9,10). It is considered a state of low-grade inflammation (11–13). CRP levels have been reported to be augmented in diabetic patients (11–13). The Munich Myocardial Infarction Registry analyzes the outcome of hospital mortality in both diabetic and nondiabetic subjects (13,14). The present study aimed at determining the role of CRP in patients with myocardial infarction and comparing the results between diabetic and nondiabetic patients.

RESEARCH DESIGN AND METHODS

All patients of the Munich Myocardial Infarction Registry (2001–2004, $n = 1,237$) were included in the analysis. Myocardial infarction was defined and treated according to the recommendations of the European Society of Cardiology and the American College of Cardiology (15,16–18).

The presence of diabetes was defined if the patient had been informed of this

diagnosis or was on prescribed anti-diabetes treatment. Patients without diagnosis but with blood glucose ≥ 200 mg/dl (3) were also classified as having diabetes (14). CRP was measured on admission and analyzed by a highly sensitive CRP-Assay, (Roche Diagnostics, Basel, Switzerland).

Statistics

Group comparisons were performed by Mann-Whitney U test for continuous variables and χ^2 test for categorical variables. Crude odds ratios (ORs) and 95% CIs were adjusted for age, sex, renal failure, and diabetes. Multiple logistic regression analysis was performed as binary logistic regression analysis after transformation of the non-normally distributed CRP levels into quintiles and dichotomization of age.

RESULTS— In the entire group of patients ($n = 1,237$), mean age was 68 ± 13 years. Thirty-seven percent presented with previously known coronary artery disease and 25% with a history of previous myocardial infarction. Sixty-four percent presented with hypertension, and 28% had an impaired kidney function. Total hospital mortality of the entire group of patients was 15.9% ($n = 210$). There were 479 patients (38.7%) who presented with diabetes.

In the entire group of patients with acute myocardial infarction, the median

(25th–75th percentile) CRP on admission was 7 mg/l (3–25). Glucose levels on admission were not significantly different between patients with CRP levels equal to or below the median compared with those with CRP levels above the median (166 ± 68 vs. 175 ± 86 mg/dl, respectively). In patients with CRP levels above the median, hospital mortality was higher compared with that for patients with CRP levels equal to or below the median (20 vs. 9%, respectively; $P < 0.001$). In patients who died in the hospital ($n = 210$), median CRP levels were higher (22 mg/l) compared with those in patients who survived (6 mg/l; $P < 0.001$).

After multiple correction for age, presence of diabetes, impairment of kidney function, hypertension, presence of reinfarction, and known peripheral arterial disease, CRP levels remained an independent predictor of hospital mortality in patients with acute myocardial infarction (highest vs. lowest quintile of CRP levels: OR [95% CI] 4.66 [2.28–9.53]; $P < 0.001$).

CRP plasma levels on admission were higher in diabetic than in nondiabetic patients: median (25th–75th percentile) 8 mg/l (3–36) vs. 6 mg/l (3–20) ($P = 0.001$). The prevalence of diabetes rose with the level of elevation of CRP plasma levels (1st quintile [2 mg/l], 38%; 2nd [3–4 mg/l], 30%; 3rd [5–9 mg/l], 35%; 4th [10–40 mg/l], 43%; and 5th [>40 mg/l], 46%; P for trend <0.01).

Diabetic patients who died in the hospital presented with higher CRP plasma levels on admission compared with those presented by diabetic patients who survived: median (25th–75th percentile) 23 mg/l (6–77) vs. 7 mg/l (2–26), respectively; $P < 0.001$. Nondiabetic patients who died in the hospital also presented with higher CRP levels compared with those in patients who survived: 16 mg/l (5–98) vs. 5 mg/l (2–17); $P < 0.001$.

Hospital mortality with regard to CRP quintiles in diabetic and nondiabetic patients are displayed in Fig. 1. In both diabetic and nondiabetic patients, CRP levels remained a significant predictor for hospital mortality after correction for age, kidney dysfunction, hypertension, reinfarction,

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Abbreviations: CRP, C-reactive protein.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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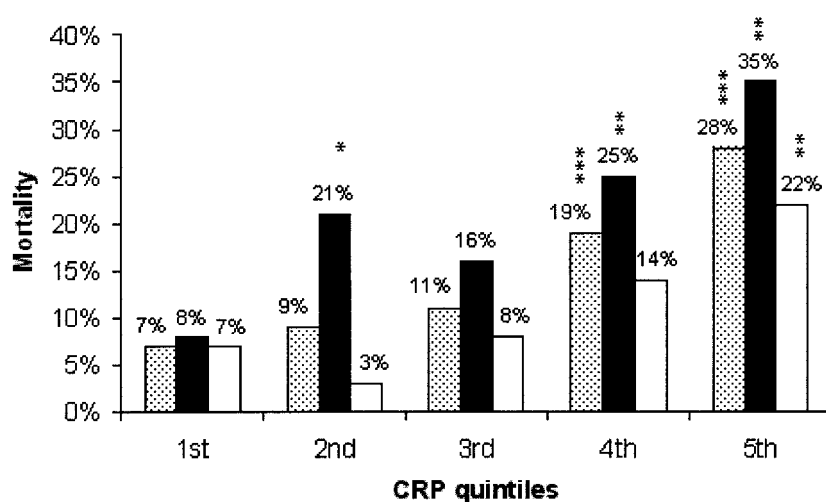


Figure 1—CRP quintiles in acute myocardial infarction (1st quintile, <3 mg/dl; 2nd, 3–4 mg/dl; 3rd, 5–9 mg/dl; 4th, 10–40 mg/dl; and 5th, >40 mg/dl). P for trend vs. lowest quintile: * $P < 0.05$; ** $P < 0.01$; and *** $P < 0.001$. ▨, entire group of patients; ■, diabetic patients; □, nondiabetic patients.

tion, and known peripheral arterial disease: for the highest versus lowest quintiles in diabetic patients, OR (95% CI) 7.15 (2.02–25.30) ($P < 0.01$); in nondiabetic patients, 3.47 (1.43–8.45) ($P < 0.01$).

In patients with CRP levels below the median and absence of both diabetes and impaired kidney function, hospital mortality was 4.8%. In patients with CRP levels above the mean and the presence of both diabetes and impaired kidney function, hospital mortality increased to 35.3% ($P < 0.001$).

CONCLUSIONS— The study of the Munich Myocardial Infarction Registry demonstrates that CRP on admission is a strong predictor for hospital mortality in both diabetic and nondiabetic patients. A cutoff of 7 mg/dl for CRP levels on admission is suggested for patients with acute myocardial infarction. In patients with CRP levels equal to or below the cutoff, hospital mortality was 9% compared with 20% in patients with CRP levels above the median ($P < 0.001$).

Diabetic patients presented with higher CRP levels compared with those in nondiabetic subjects. Furthermore, the prevalence of diabetes increased significantly with quintiles of CRP levels.

The standard cutoff for CRP has been reported to be 5 mg/l (4). The use of this cutoff level, however, does not incorporate the overall CRP elevation in acute myocardial infarction, which is considered to occur as a result of the acute event (19,20). The Munich Myocardial Infarction Registry, which investigates patients

with troponin-positive myocardial infarction with and without ST elevation, suggests the use of a 7 mg/dl cutoff for CRP levels. Previously, Lim et al. (21) suggested CRP levels of 10 mg/l and Dibra et al. (22) CRP levels >12 mg/l to detect acute myocardial infarction patients at increased risk for short- and long-term mortality. In the two studies, however, only 147 and 250 patients were included.

In the Munich Myocardial Infarction Registry, the combined presence of diabetes and CRP levels in the two upper quintiles demonstrated that the rate of mortality was six- to sevenfold higher than that in diabetic patients who presented with CRP levels in the lowest tertile. The relationship between atherothrombosis, inflammation, and diabetes is supported in the clinical setting of a registry (23,24).

The Munich Myocardial Infarction Registry emphasizes the importance of CRP levels on admission with regard to the hospital outcome of diabetic and nondiabetic patients. A 7 mg/dl cutoff for CRP levels on admission is suggested for patients with acute myocardial infarction. The excessive risk of mortality in patients with diabetes and elevated CRP will require an intensification of strategies to overcome the poor prognosis.

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