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The Relation between Preprocedural C-Reactive Protein Levels and Early and Late Complications in Patients with Acute Myocardial Infarction Undergoing Interventional Coronary Angioplasty

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Summary

Background: Inflammation is an important feature of arteriosclerotic disease, and the vulnerability of coronary plaques in acute myocardial infarction (AMI) may be related to the levels of serum C-reactive proteins (CRP). While some risk factors for early and late complications have been suggested, an accurate and definitive preprocedural risk stratification of patients undergoing percutaneous transluminal coronary angioplasty (PTCA) is still lacking.

Hypothesis: The study was undertaken to investigate whether early and late complications after PTCA could be predicted by evaluation of baseline serum CRP levels in patients with AMI.

Methods: Levels of serum CRP were measured in a total of 230 patients with AMI undergoing PTCA and provisional stent. They were divided into two groups: Group 1 (n = 48) with elevated CRP levels (≥ 5 mg/l) and Group 2 (n = 182) with normal CRP levels (< 5 mg/l).

Results: There were no significant differences in baseline clinical, angiographic, and procedural characteristics between the two groups. However, the incidence of in-hospital adverse coronary events (reinfarction, coronary reocclusion, target vessel revascularization, and death) and severe left ventricular dysfunction was significantly higher in Group 1 (18.3 vs. 6.1%, $p < 0.05$ and 20.9 vs. 6.1%, $p < 0.05$, respectively). In addition, bailout stenting was performed more frequently in Group 1 than in Group 2 (60.4 vs. 36.3%, $p < 0.005$). No significant late complications were noted. The serum levels of CRP were the only independent predictors of early adverse events.

Conclusions: Preprocedural serum CRP level might be considered a powerful predictor of early but not late complications in patients undergoing PTCA/stent procedures.

Key words: inflammation, C-reactive protein, coronary artery disease, percutaneous transluminal coronary angioplasty/stent, major adverse cardiac events, left ventricular ejection fraction, restenosis

Introduction

Pathophysiologic understanding of coronary artery lesions in acute myocardial infarction (AMI) actually appears to be of extreme importance, because coronary interventional angioplasties for patients with AMI are being applied more frequently than ever.[1]

Inflammation is an important feature of atherosclerotic lesions, and the site of plaque rupture in AMI is invariably associated with the occurrence of regional accumulation of activated lymphocytes and monocytes/macrophages.[2] One of the characteristic features of inflammation is an increase in the circulating concentrations of cytokines and acute phase reactants such as C-reactive protein (CRP), serum amyloid A protein, and fibrinogen.[3] The CRP, an easily measurable acute phase reactant, which is synthesized by the liver in response to proinflammatory stimulation by cytokines such as interleukin-6, has been confirmed to be a sensitive predictor and is associated with worse prognosis for coronary artery disease (CAD).[3–5]

Normal CRP levels had a 100% negative predictive value for early adverse events in patients post AMI and identified a subset of patients (43% of the whole population) who did not require additional treatment until hospital discharge.[6–8]

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Percutaneous transluminal coronary angioplasty (PTCA) with or without stent implantation is an established revascularization procedure; however, restenosis rates still range between 30–60%[6] and 15–30%,[7] respectively

Preprocedural identification of low- and high-risk patients who might benefit from additional procedures[6, 8] would be desirable. However, the predictors of early[7–10] and late complications[11–15] have a low predictive value,[15–18] are available only after procedures,[9, 14] or are not easily applicable in clinical practice.[10, 12, 13] Inconsistent and weak correlation with early complications following PTCA was reported for female gender, extreme age, diabetes, multivessel disease, lesion characteristics, and hemostatic variables.[6–18]

This study was therefore undertaken to investigate the short- and long-term prognostic value of preprocedural serum levels of CRP in patients with AMI receiving PTCA/stenting.

Methods

Patients

The study population comprised 230 of 268 consecutive patients with ST-elevation AMI who were admitted to our departments between January 1999 and June 2002 and underwent PTCA to the infarct-related coronary artery (Table I). These patients fulfilled the following AMI criteria: typical chest pain of > 30 min duration, significant ST-T segment elevation of > 0.1 Mv in limb leads and > 0.2 Mv in more than two adjacent precordial leads, and peak creatine kinase levels of more than twice the upper limit of normal.

All patients with AMI who were admitted to our departments were included in this study; subsequently we excluded those who had previous PTCA or coronary artery bypass graft surgery (CABG) (n = 17) (because patients with postinterventional modalities and chronic CAD are much more likely to develop early/late complication than others), intercurrent inflammatory conditions (n = 16), and left bundle-branch block (n = 5). These, however, were followed as study patients for 1 additional year. At the time they underwent PTCA procedure, all patients were receiving oral aspirin and ticlopidin (ticlidil)/clopidogrel, and they received heparin at a dose required to maintain the activated clotting time > 300 s throughout the procedure, followed by 500 U/h for 24 h.

Written informed consent was obtained from all patients and the protocol was approved by the institutional committees.

Blood Sampling and Laboratory Assays

Peripheral blood samples for CRP were taken before PTCA/stenting procedures by direct venipuncture after minimal venostasis. Coded plasma samples were stored at −70C and analyzed in a single batch at the end of the study; thus, patient management was independent of these results. C-reactive protein was assayed using a highly sensitive method, the latex-enhanced nephelometry with a Behring Nephlometer Analyzer System (Behring Diagnostics, Inc.) and an NA Latex CRP Kit (Behring Diagnostics, Inc., Weisbaden, Germany).[19, 20] Quality control was carried out with daily runs of diluted standards prepared by Behring Diagnostics and standardized against the

TABLE I Clinical, angiographic, and procedural characteristics

	Group 1 (n = 48)	Group 2 (n = 182)
Age, years	62 ± 8	64 ± 9
Male, n (%)	37 (77)	140 (71)
Systemic hypertension, n (%)	26 (55)	91 (50)
Diabetes mellitus, n (%)	12 (25)	54 (29)
Hypercholesterolemia (> 200 mg/dl), n (%)	14 (29)	58 (30)
Smokers, n (%)	38 (79)	150 (72)
Previous MI, n (%)	4 (7)	12 (6)
Location of MI		
Anterior, n (%)	40 (84)	140 (71)
Lateral, n (%)	3 (6)	14 (7)
Inferior, n (%)	5 (10)	28 (22)
Multivessel disease, n (%) [a]	20 (40)	70 (39)
Collateral, n (%)	10 (20)	40 (21)
Dilated coronary artery		
Left anterior descending, n (%)	30 (62)	102 (56)
Left circumflex, n (%)	14 (28)	70 (39)
Right coronary artery, n (%)	4 (10)	10 (5)
Target stenosis pre PTCA/stenting		
Percent diameter, %	77 ± 13	80 ± 9
Minimal lumen diameter, mm	0.7 ± 0.2	0.6 ± 0.2
Type E2, % [b]	38	72
Type B2-C, % [c]	62	28
Small vessel (< 3.0 mm), %	69	52
No-reflow, n (%)	2 (4)	10 (5)
TIMI flow (post PTCA/stenting):		
3, n (%)	44 (90)	168 (93)
2, n (%)	2 (5)	11 (5)
1, n (%)	2 (5)	3 (2)
Inflation pressure, atm	6.6 ± 1.8	6.4 ± 2.2
Total inflation time, s	456 ± 235	432 ± 212
Balloon/vessel ratio	1.1 ± 0.1	1.1 ± 0.1
Acute gain, mm	1.3 ± 0.6	1.0 ± 0.5
PTCA/stenting success, n (%)	47 (98)	78 (97)
Target stenosis post PTCA/stenting		
Percent diameter, %	30 ± 10	28 ± 12
Minimal lumen diameter, mm	2.0 ± 0.6	2.2 ± 0.3
Time to initial CRP, h	36 ± 4.5	40 ± 3.2
Time to PTCA/stenting, h	36 ± 4.5	40 ± 3.2

[a] Presence of > 75% diameter stenosis in two or three major epicardial vessels.

[b] Ambrose *et al.*[35] classification.

[c] Modified scheme from American College of Cardiology/American Heart Association Task Force classification.[16]

Values are mean ± SD or n (%). P not significant for any variable.

Abbreviations: MI = myocardial infarction, PTCA = percutaneous transluminal coronary angioplasty, TIMI = Thrombolysis in Myocardial Infarction, CRP = C-reactive protein, SD = standard deviation.

World Health Organization (WHO) reference preparation of CRP serum. The range of values detected by the assay is 0 to 48 mg/l. With this method, the median normal value of CRP (2–5 mg/l) in 100% of normal healthy volunteers,[21] conforms to a previous report using different methods.[22]

Angiographic Studies

The procedure was performed in all patients using a steerable balloon catheter system through the femoral or brachial artery. Selective coronary angiography was performed in multiple projections before interventional coronary angiography procedures. Coronary artery stenosis was classified according to American Heart Association (AHA) classification.[23] Coronary artery stenosis of ≥ 75% was considered significant. Collateral circulation was classified according to Rentrop grading[24] and was considered significant if the grade was ≥ 2. Procedural angiograms were also analyzed for Thrombolysis In Myocardial Infarction (TIMI) flow grade,[25] the appearance of intracoronary thrombi (intraluminal filling defects or contrast medium staining within the lumen), and luminal dissection.[16] Because of local circumstances, while the patients were completely asymptomatic, PTCA was performed 36 ± 4.5 h after onset of AMI in all patients who had ≥ 75% coronary artery stenosis, using standard technique and equipment and confining it to the infarct-related artery.

Coronary stenting as a primary procedure was performed in 10% of patients and was performed as a bailout procedure in 102 patients for coronary dissection and/or suboptimal dilation (≥ 50% residual stenosis after several 60–90 second balloon inflations). Contrast left ventriculography was performed routinely in all patients, and left ventricular ejection fraction (LVEF) was calculated by the area-length method. Percutaneous transluminal coronary angioplasty was considered successful if the final percent diameter stenosis was < 50% with TIMI grade 3 flow in the absence of recurrent ischemia, MI (creatine kinase increase to more than twice the upper limit of normal with or without evidence of new Q waves), need of bailout stenting or urgent CABG during hospitalization, or death. Angiographic restenosis was defined as > 50% stenosis of the culprit lesion dilated by coronary intervention, as evaluated by quantitative coronary analysis. After the procedure, all patients underwent creatine kinase evaluations every 6 h for 48 h, and daily recording of symptoms and electrocardiogram (ECG) was undertaken until hospital discharge (5 ± 2 days after the procedure). All patients received aspirin and ticlopidine (ticlidil)/clopidogrel (plavix) on discharge; calcium antagonists and other drugs were ordered if clinically indicated. Clinical follow-up visits and treadmill stress tests were scheduled at 1, 3, 6, and 12 months. Coronary angiography was repeated in patients with evidence of clinical restenosis, which was defined as the recurrence or worsening of ischemic symptoms (typical angina and MI) or ischemia at exercise testing (> 1 mm ST-segment depression). The following early complications were considered as early adverse events: (1) abrupt occlusion, defined as an acute flow reduction (TIMI 0–1); (2) threatened abrupt occlusion, defined as luminal dissection (type D–E)[16] or new thrombus appearance with delayed runoff of contrast, or TIMI grade ≤ 2 flow; and (3) early recurrence of ischemia, defined as rest angina associated with transient ECG signs of ischemia or MI before hospital discharge.

Late complication was defined as clinical evidence of restenosis during the year following hospital discharge.

The need for repeat coronary angiography, PTCA, or CABG was also evaluated.

Statistical Analysis

Categorical data were compared by chi-square test. The Student's *t*-test was used to compare continuous variables. Linear regression analysis was used to assess possible correlation among CRP and LVEF. Multiple logistic regression analysis was applied to examine the determinants of major adverse in-hospital coronary events. A p value of < 0.05 was considered significant.

Results

Patients were classified into two groups: Group 1 (n = 48), with elevated CRP levels (≥ 5 mg/dl), and Group 2 (n = 182), with normal CRP levels. Clinical characteristics, angiographic findings, and procedural variables are shown in Table I.

Outcomes for each group are shown in Table II and Figure 1. The incidence of acute or subacute coronary reocclusion after primary PTCA/stenting was significantly higher in Group 1 than in Group 2 (14.7 vs. 2.8%, $p < 0.05$). In addition, there was a significant difference in the incidence of reinfarction (18.5 vs. 6.6%, $p < 0.05$). Similarly, the incidence of early-phase target vessel revascularization was significantly more frequent in Group 1 than in Group 2 (10.4 vs. 2.3%, $p < 0.05$). Bailout stenting implantation was also more frequent in Group 1 than in Group 2 (60.4 vs. 37.6%, $p < 0.005$). The incidence of heart failure (acute pulmonary edema and/or cardiogenic shock) was significantly higher in Group 1 than in Group 2 (20.9 vs. 6.1%, $p < 0.05$). In-hospital mortality rate was significantly higher in Group 1 than in Group 2 (20.9 vs. 2.3%, $p < 0.01$). Thus, the rate of major adverse cardiac events (reinfarction, target vessel revascularization, and death) was significantly higher in Group 1 than in Group 2 (18.3 vs. 1%, $p < 0.05$). The majority of in-hospital deaths in Group 1 was related to heart failure in eight patients (80%), and in the remaining two patients (20%) it was associated with acute or subacute coronary reocclusion; causes of in-hospital death in Group 2 were reinfarction in seven (63.7%), heart failure in one (9%), and sudden death in three patients (27.3%). There was no significant difference in the incidence of major adverse cardiac events between those who received stenting (7.7%) and those who did not (7.4%). One-year follow-up was completed in all patients, and no significant differences in the incidence of target vessel restenosis and revascularization and deaths were found among them.

The results of clinical measurements are summarized in Table II. There were significant differences in serum CRP

TABLE II Clinical events and measurements.

	Group 1 (n = 48)	Group 2 (n = 182)	p Value
Early complications			
Reinfarction, n (%)	9 (18.5)	12 (6.6)	< 0.05
Coronary reocclusion, n (%)	7 (14.7)	5 (2.8)	< 0.05
Rest angina, n (%)	3 (6.2)	5 (2.7)	NS
Target vessel revascularization, n (%)	5 (10.4)	4 (2.3)	< 0.05
Bailout stenting, n (%)	29 (60.4)	68 (36.3)	< 0.005
Pulmonary edema/shock, n (%)	10 (20.9)	11(6.1)	< 0.05
Major adverse cardiac events, n (%) [a]	9 (18.3)	11 (6.1)	< 0.05
Death, n (%)	10 (20.9)	4 (2.3)	< 0.05
Late complications (during 1-year follow-up)			
Restenosis, n (%)	2 (4.1)	12 (6.6)	NS
Target vessel revascularization, n (%)	1 (2.1)	5 (2.7)	NS
Death, n (%)	2 (4.1)	3 (1.6)	NS
Clinical measurements			
CRP levels, mg/dl	13.8 ± 3.7	3.1 ± 1.1	< 0.05
Left ventricular ejection fraction, %	35 ± 10.3	48 ± 9.2	< 0.05

Values are n (%), and mean ± SD.
[a] In-hospital reinfarction, target vessel revascularization, and/or death.
Abbreviation: NS = not significant. Other abbreviations as in Table I.

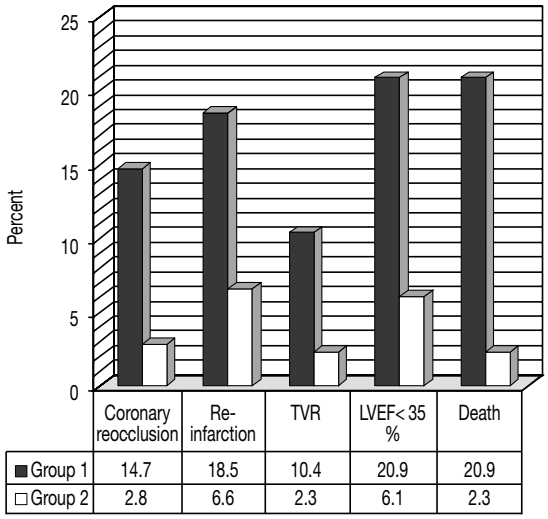

FIG. 1 In-hospital adverse coronary events. TVR = target vessel revascularization, LVEF = left ventricular ejection fraction. p < 0.05.

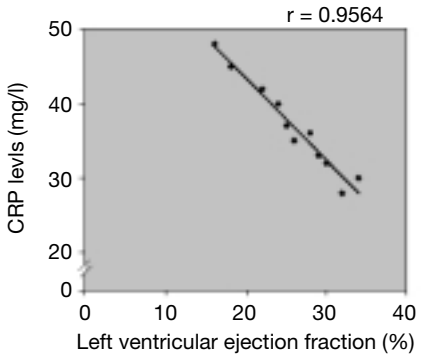

FIG. 2 Correlation between C-reactive protein (CRP) levels and left ventricular ejection fraction in patients of both groups. ◆ = Group 1 (distribution), ——— = Group 1 (linear).

levels (13.8 ± 3.7 vs. 3.1 ± 1.1 mg/dl, p < 0.05) and in left ventricular dysfunction occurrences (LVEF 35 ± 10.3% vs. 48 ± 9.2%, p < 0.05) between the two groups. A significant inverse correlation was found between the abundantly high CRP levels and the severity of left ventricular dysfunction in the patients of both groups (r = 0.279, p < 0.01) (Fig. 2).

The results of multivariate analysis are summarized in Table III. The serum CRP level was the only significant independent predictor of in-hospital repeat PTCA/stenting and major adverse cardiac events (including acute and subacute coronary reocclusion, heart failure, target vessel revascularization, reinfarction, and death) (p < 0.005). In contrast, none of the other clinical characteristics, such as age, gender, coronary risk factors, previous MI, unstable angina before onset of MI, location of MI, multivessel disease, collaterals, initial coronary flow, no-reflow, TIMI flow after PTCA/stenting procedure, PTCA/stenting success, and time from onset of MI to primary PTCA/stenting procedure was a significant determinant of adverse cardiac events among hospital in-patients.

Discussion

Pathologic studies have indicated that unstable coronary plaque is constituted by a thin cap and weak shoulder with ex-

TABLE III Multiple logistic analysis

	Odds ratio	95% CI	p Value
CRP levels ≥ 5 mg/dl	7.7	2.16–22.30	0.0015
Anterior MI	2.28	0.64–8.46	NS
Hypertension	2.08	0.61–7.50	NS
Initial coronary flow	2.22	0.58–8.21	NS
Multivessel disease	1.74	0.52–6.81	NS

Abbreviations: CI = confidence intervals, MI = myocardial infarction, NS = not significant.

cessive inflammatory cell infiltration.[17] Previous studies, such as those by Abdelmouttaleb *et al.*,[4] Liuzzo *et al.*,[5] Koenig *et al.*,[26] and Ridker *et al.*[27] have demonstrated that in cardiovascular disease, serum CRP correlated positively with the extent and severity of atherosclerosis disease. Based on the abovementioned data, inflammatory activity and vulnerability of coronary lesions could be estimated by the measurement of CRP levels before performing the PTCA/stenting procedure.

This prospective study is not the first to provide evidence that, in a consecutive group of patients undergoing PTCA/stenting to the culprit lesion, early complications can be predicted with reasonable accuracy by CRP measurements prior to the PTCA/stenting procedure. In this study it was noted that about one-third of the patients with increased CRP levels (> 5 mg/dl) (Table III) had early adverse cardiac events, while < 5% of those with normal CRP levels (Group 2) had these complications. In addition, we found that, while patients with mild to moderately high CRP levels (> 5–< 15 mg/dl) developed more acute or subacute coronary reocclusion, coronary revascularization, and reinfarction, those with abundantly high CRP levels (> 20 mg/dl) had more incidents of significantly reduced LVEF (< 35%) and death. The incidence of significant inverse correlation between the CRP concentration and LVEF in Group 1 could be related to the size/site of the MI (antero-septal MI in 84% of Group 1 patients vs. 71% in Group 2 patients).

Previous studies reported that in clinical practice, unstable angina is the most important predictor of early complications following PTCA/stenting;[7, 8, 28–30] however, our observation that serum CRP levels before the PTCA/stenting procedure are even stronger predictors of early complications suggests that the degree of activation of inflammatory cells is a more important determinant of early outcome after PTCA/stenting than clinical instability.

Our results are consistent with the recent observation of Gaspardone *et al.*,[31] who suggested that preprocedural activation of inflammatory cells may influence intimal instability and further early coronary complications. In addition, they are consistent with the study by Tomoda *et al.*,[32] who reported similar findings regarding the post-PTCA/stent early complication, but without relation to the time of blood drawn for CRP evaluation. However, the observation of Buffon *et al.*,[33] who suggested that the serum levels of CRP before PTCA/stenting procedure correlate positively with the post-PTCA/stent late complications, such as coronary restenosis, was not demonstrated in our population during the 1-year follow-up.

Study Limitations

The study was conducted in a relatively small number of patients (and events). However, the prognostic value of this marker, if proven in larger clinical studies, could contribute to optimizing therapeutic resources in the complex scenario of interventional cardiology.[34] Another limitation of our study is the lack of repeat angiography in asymptomatic patients. However, an increasing number of published and ongoing studies are focusing only on clinical features. In addition, our study lacks the usefulness of other evolving new technologies, except the platelet glycoprotein IIb/IIIa receptor blockade (plavix).

Conclusions

Our study has shown that serum levels of CRP before PTCA/stenting may provide a more powerful predictor of early but not late coronary complications than do clinical presentation and other risk factors considered so far. In addition, it has shown that abundantly high levels of CRP could correlate significantly with severely reduced LVEF incidence. Our observation that high incidence of severe left ventricular dysfunction significantly correlates with the abundantly high serum levels of CRP stresses the need for large studies to evaluate this issue.

References

1. Stone GW, Brodie BR, Griffin JJ, for the PAMI Stent Pilot Trial Investigators: Clinical and angiographic follow-up after primary stenting in acute myocardial infarction. The Primary Angiography in Myocardial Infarction (PAMI) Stent Pilot Trial. *Circulation* 1999;99:1548–1554
2. Ross R: The pathogenesis of atherosclerosis: A perspective for the 1990s. *Nature* 1993;362:801–809
3. Baumann H, Gauldie J: Regulation of hepatic acute phase plasma protein genes by hepatocyte stimulating factors and other mediators of inflammation. *Mol Biol Med* 1990;7:147–159
4. Abdelmouttaleb I, Danchin N, Ilardo C: C-reactive protein and coronary artery disease: Additional evidence of the implication of an inflammatory process in acute coronary syndrome. *Am Heart J* 1999;137:346–351
5. Liuzzo G, Biasucci LM, Gallimore JR: Prognostic value of C-reactive protein and plasma amyloid A protein in severe unstable angina. *N Engl J Med* 1994;331:417–424
6. Macaya C, Serruys PW, Ruygrok P: Continued benefit of coronary stenting versus balloon angioplasty: One-year clinical follow-up of Benestent trial. Benestent Study Group. *J Am Coll Cardiol* 1996;27:255–261
7. Detre KM, Holmes DR Jr, Holubkov R: Incidence and consequences of periprocedural occlusion of the 1985–1986 National Heart, Lung, and Blood Institute's Percutaneous Transluminal Coronary Angioplasty registry. *Circulation* 1990;82:739–750
8. de Feyer PJ, Ruygrok PN: Coronary intervention: Risk stratification and management of abrupt coronary occlusion. *Eur Heart J* 1995;16(suppl L): L97–103
9. Oltrona L, Eisenberg PR, Lasala JM. Sewall DJ, Shelton ME, Winters KJ: Association of heparin resistant thrombin activity and acute ischemic complications of coronary interventions. *Circulation* 1996;94:2064–2071
10. Tschoepe D, Schultheiss HB, Kolarov P: Platelet membrane activation markers are predictive for increased risk of acute ischemic events after PTCA. *Circulation* 1993;88:37–42

11. Rensing BJ, Hermans WRM, Vos J: Luminal narrowing after percutaneous coronary angioplasty: A study of clinical, procedural, and lesional factors related to long-term angiographic outcome. *Circulation* 1993;88:975–985
12. Ishiwata S, Tukada R, Nakanishi S, Nishiyama S, Seki A: Postangioplasty restenosis: Platelet activation and the coagulation-fibrinolysis system as possible factors in the pathogenesis of restenosis. *Am Heart J* 1997;133: 387–392
13. Pietersma A, Kofflard M, de Wit EA: Late luminal loss after coronary angioplasty is associated with the activation status of circulating phagocytes before treatment. *Circulation* 1995;91:1320–1325
14. Montalescot G, Ankri A, Vicaut E, Drobinski G, Grosgogeat Y, Thomas D: Fibrinogen after coronary angioplasty as a risk factor for restenosis. *Circulation* 1995:92:31–38
15. Desmarais RL, Sarembock IJ, Ayers CR, Vernon SM, Powers ER, Gimple LW: Elevated serum lipoprotein(a) is a risk factor for clinical recurrence after coronary balloon angioplasty. *Circulation* 1995;91:1403–1409
16. Tan K, Sulke N, Sowton E: Clinical and lesion morphologic determinants of coronary angioplasty success and complications: Current experience. *J Am Coll Cardiol* 1995;25:855–865
17. Cermak J, Key NS, Bach RR, Balla J, Jacob HS Vercellotti GM: C-reactive protein induces human peripheral blood monocytes to synthesize tissue factor. *Blood* 1993;82:513–520
18. Galis ZS, Muszynski M, Sukhova GK, Simon-Morrissey E, Lippy P: Enhanced expression of vascular matrix metalloproteinases induced in vitro by cytokines and in regions of human atherosclerotic lesions. *Ann NY Acad Sci* 1995;748:501–507
19. Wilkins J, Gallimore JR, Tennent GA: Rapid automated enzyme immunoassay of serum amyloid A. *Clin Chem* 1994;40:1284–1290
20. Centers for Disease Control and Prevention: Plan and operation of the Third National Health and Nutrition Examination Survey. 1988–94. Bethesda, Md.: National Center for Health Statistics; 1994. Vital Health Statistics 1(32). Series 1, No. 32
21. Abbot Laboratories Instruction Manual. Protein C-reactive TDx/TDxFLx. Abbot Laboratories, North Chicago, Ill.
22. Shine B, DE Beer FC, Pepys MB: Solid phase radioimmunoassay for CRP. *Clin Chim Acta* 1981;117:13–23
23. Austen WG, Eduards JE, Frye RL: A reporting system on patients evaluated for coronary artery disease. *Circulation* 1975;51:7–40
24. Rentrop KP, Cohen M, Bianke H: Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. *J Am Coll Cardiol* 1985;5:587–592
25. The TIMI Study group: The Thrombolysis in Myocardial Infarction (TIMI) trial. *N Engl J Med* 1985;312:932–936
26. Koenig W, Sund M, Frohlich M: C-reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men. Results from the MONICA (Monitoring Trends and Determinations in Cardiovascular Disease) Ausborg cohort study, 1984 to 1992. *Circulation* 1999;99:237–242
27. Ridker PM, Cushman M, Stampfer MJ: Plasma concentration of C-reactive protein and risk of developing peripheral vascular disease. *Circulation* 1998; 97:425–428
28. Ellis SG, Vandormael MG, Cowley MJ: Coronary morphologic and clinical determinants of procedural outcome with angioplasty or multivessel coronary disease. Implications for patient selection. *Circulation* 1990;82:1193–1202
29. White CJ, Ramee SR, Collins TJ: Coronary thrombi increase PTCA risk. Angioscopy as a clinical tool. *Circulation* 1996;93:253–258
30. Lincoff AM, Popma JJ, Ellis SG, Hacker JA, Topol EJ: Abrupt vessel closure complicating coronary angioplasty: Clinical, angiographic and therapeutic profile. *J Am Coll Cardiol* 1992;19:926–935
31. Gaspardone A, Crea F, Versaci F: Predictive value of C-reactive protein after successful coronary artery stenting in patients with stable angina. *Am J Cardiol* 1998;82:515–518
32. Tomoda H, Aoki N: Prognostic value of C-reactive protein levels within six hours after the onset of acute myocardial infarction. *Am Heart J* 2000;140: 324–328
33. Buffon A, Liuzzo G, Biasucci LM: Preprocedural serum levels of C-reactive protein predict early complications and late restenosis after coronary angioplasty. *J Am Coll Cardiol* 1999;34:1512–1521
34. The Epilog Investigators: Platelet glycoprotein IIb/IIIa receptor blockade and low-dose heparin during percutaneous coronary revascularization. *N Engl J Med* 1997;336:1689–1696
35. Ambrose JA, Winters SL, Arora AA: Coronary angiographic morphology in myocardial infarction: A link between pathogenesis of unstable angina and myocardial infarction. *J Am Coll Cardiol* 1985;6:1233–1238