

MULTIPLE COMPLEX CORONARY PLAQUES IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Background Acute myocardial infarction is believed to be caused by rupture of an unstable coronary-artery plaque that appears as a single lesion on angiography. However, plaque instability might be caused by pathophysiologic processes, such as inflammation, that exert adverse effects throughout the coronary vasculature and that therefore result in multiple unstable lesions.

Methods To document the presence of multiple unstable plaques in patients with acute myocardial infarction and determine their influence on outcome, we analyzed angiograms from 253 patients for complex coronary plaques characterized by thrombus, ulceration, plaque irregularity, and impaired flow.

Results Single complex coronary plaques were identified in 153 patients (60.5 percent) and multiple complex plaques in the other 100 patients (39.5 percent). As compared with patients with single complex plaques, those with multiple complex plaques were less likely to undergo primary angioplasty (86.0 percent vs. 94.8 percent, $P=0.03$) and more commonly required urgent bypass surgery (27.0 percent vs. 5.2 percent, $P\leq 0.001$). During the year after myocardial infarction, the presence of multiple complex plaques was associated with an increased incidence of recurrent acute coronary syndromes (19.0 percent vs. 2.6 percent, $P\leq 0.001$); repeated angioplasty (32.0 percent vs. 12.4 percent, $P\leq 0.001$), particularly of non-infarct-related lesions (17.0 percent vs. 4.6 percent, $P\leq 0.001$); and coronary-artery bypass graft surgery (35.0 percent vs. 11.1 percent, $P\leq 0.001$).

Conclusions Patients with acute myocardial infarction may harbor multiple complex coronary plaques that are associated with adverse clinical outcomes. Plaque instability may be due to a widespread process throughout the coronary vessels, which may have implications for the management of acute ischemic heart disease. (N Engl J Med 2000;343:915-22.)

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RUPTURE of coronary-artery plaques, resulting in thrombotic occlusion, is implicated in the pathogenesis of acute myocardial infarction.¹⁻⁶ Plaque disruption is thought to be a function of the interplay between factors intrinsic to the plaque and extrinsic forces.³⁻⁵ However, the specific mechanisms mediating plaque instability have not been fully delineated.

Plaque rupture is thought to reflect local plaque instability attributable to spontaneous or triggered disruption of a vulnerable plaque that is manifested angiographically or pathologically as a single complex

lesion. However, the pathophysiologic factors that are believed to precipitate plaque rupture — whether as a result of primary weakening of the fibrous cap attributable to inflammation^{3,4,7-9} or as a result of the extrinsic influences of intraluminal mechanical forces modulated by sympathetic tone and catecholamines^{10,11} — might reasonably be expected to exert their effects in a widespread pattern throughout the coronary vasculature. Given the potentially widespread effect of these factors that adversely influence plaques, together with the typically diffuse nature of coronary atherosclerosis,¹² plaque instability might be expected to develop in a multifocal pattern, resulting in multiple complex, unstable plaques in anatomically remote locations; any one of these lesions might progress to total occlusion of a vessel and emerge as the cause of an infarct.

This angiographic study was designed to document the incidence of multiple complex plaques in patients with acute transmural myocardial infarction and to determine their influence on clinical outcome.

METHODS**Study Design**

We analyzed angiograms from 253 consecutive patients with acute transmural myocardial infarction. All the patients were treated with aspirin (325 mg orally), heparin (10,000 units by intravenous bolus), intravenous nitroglycerin, and beta-blockers, unless contraindicated. Coronary angiography, left ventricular cineangiography, and angioplasty were performed by standard techniques.¹³ The study protocol was approved by the hospital's institutional review board.

Angiographic Analysis

Coronary angiograms were analyzed as previously described, with substantial lesions (those that narrowed the diameter of the vessel by 50 percent or more) measured by quantitative analysis.¹³ Complex coronary plaques were identified according to previously used criteria¹⁴⁻¹⁶: an intraluminal filling defect consistent with thrombus, defined as abrupt vessel cutoff with persistence of contrast, or an intraluminal filling defect in a patent vessel within or adjacent to a stenotic region with surrounding homogeneous contrast opacification; plaque ulceration, defined by the presence of contrast and hazy contour beyond the vessel lumen; plaque irregularity, defined by irregular margins or overhanging edges; and impaired flow.¹³ Lesions were considered complex if they caused at least 50 percent stenosis and had two or more of these morphologic features. Care was taken to exclude lesions characteristic of chronic total occlusion, which were identified as tapering lesions with multiple fine collaterals.

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The location of the infarct-related plaque was determined by correlating the presence of a complex plaque with electrocardiographic and wall-motion abnormalities. For each patient, the coronary vasculature was reviewed to identify anatomically remote complex plaques. An anatomically remote plaque was defined as one in a different artery from the artery containing the infarct-related plaque; in the same artery as that containing the infarct-related plaque, but in a different branch; or in the same artery and branch as the infarct-related plaque, but at least 5 cm from the infarct-related plaque, with an intervening segment of disease-free vessel. As in previous studies,¹⁴ the angiograms were analyzed by two independent angiographers, the results were compared, and when there was disagreement, a final decision was made by consensus.

Clinical Outcomes

The patients' records and the hospital data base were reviewed to analyze clinical variables, in-hospital outcomes, and the clinical course over the 12 months after myocardial infarction. The clinical information that was analyzed included the use or nonuse of aspirin, smoking status, and the presence or absence of diabetes, hypertension, and hypercholesterolemia. Information was obtained about the initial revascularization strategy; recurrent acute coronary syndromes, including unstable angina and myocardial infarction; repeated catheterization; repeated revascularization; and death. Data from patients who required a second percutaneous revascularization procedure were analyzed to determine whether the later intervention was performed on the index culprit lesion or, if it was performed on a remote plaque, whether this subsequent target had been previously designated as complex.

Statistical Analysis

Patients were divided into two groups according to whether they had single or multiple complex coronary plaques. Base-line demographic characteristics, angiographic variables, clinical variables, and outcomes were compared between these two groups. A separate analysis of patients with multivessel disease was performed, in which the same variables were compared in patients with single complex plaques and those with multiple complex plaques. Numerical variables are reported as means \pm SD. Frequencies and percentages are given for categorical variables. These variables were compared by chi-square test when applicable and otherwise by Fisher's exact test. For continuous variables, statistical comparisons were made with use of the two-tailed *t*-test, and a *P* value of less than 0.05 was considered to indicate statistical significance.

To examine whether the presence of multiple complex coronary plaques was independently predictive of clinical events, multivariate analyses were completed for one-year outcomes, including recurrent acute coronary syndromes, repeated catheterization, repeated angioplasty, and coronary bypass surgery, as well as the combined outcome of multiple adverse cardiac events, defined as the occurrence of one or more of the preceding events or of death from cardiac causes. The covariates included were the presence or absence of multiple complex plaques, age, and sex.

A step-down multivariate analysis was then completed for each of these five outcomes. The covariates included were the presence or absence of multiple complex plaques, age, sex, presence or absence of a history of hyperlipidemia, presence or absence of diabetes, left ventricular ejection fraction, and smoking status. All covariates were included initially. The least significant variable was then dropped from the model at each step until the final model included only variables with a *P* value of less than 0.05.

RESULTS

A single complex coronary plaque was identified angiographically in 153 patients (60.5 percent), and multiple complex plaques were identified in the 100 remaining patients (39.5 percent) (Table 1). The observers initially disagreed about the classification of

25 of 370 lesions (6.8 percent). Patients with single and multiple complex plaques did not differ significantly in mean age (63 ± 12 vs. 64 ± 11 years, respectively), sex ratio (67 percent vs. 69 percent male), or the frequency of coronary risk factors, including current smoking, diabetes mellitus, and hypercholesterolemia. There were no differences between the groups in the proportion with a history of infarction or angina.

Angiographic Results

The prevalence of multivessel coronary disease was lower in patients with single complex coronary plaques than in those with multiple complex coronary plaques (74.5 percent vs. 91.0 percent, $P \leq 0.001$). Patients with multiple complex plaques had a lower left ventricular ejection fraction at base line (38 ± 14 percent vs. 45 ± 14 percent, $P = 0.003$). The culprit lesion responsible for acute myocardial infarction was clearly delineated in all patients with a single complex plaque. Among those with multiple complex plaques, 83 patients (83.0 percent) had two complex plaques (Fig. 1 and 2), and 17 others (17.0 percent) had three or more complex plaques.

The complex plaque responsible for the acute myocardial infarction was clearly identified in 98 patients with multiple complex plaques (98.0 percent); in the other 2 patients (2.0 percent), it was not possible to determine which plaque was responsible. In one of the latter two patients, who had acute inferior myocardial infarction and angiographic evidence of complete thrombotic occlusion in both the circumflex and right coronary arteries (Fig. 2), angiography documented the presence of thrombus superimposed on ulcerated plaques in both vessels.

There were no differences between the groups in the angiographic appearance of the infarct-related plaque with respect to the initial percentage of stenosis, flow grade, or presence of intracoronary thrombus. In those with multiple complex plaques, the degree of stenosis of the non-infarct-related plaque tended to be less than that of the infarct-related plaque (82 ± 14 percent vs. 95 ± 7 percent, $P < 0.003$). However, the non-infarct-related plaque was associated with impaired flow in 27.0 percent of cases and with total occlusion in 10.0 percent.

In-Hospital Outcomes

Primary angioplasty of the infarct-related artery was performed in 145 (94.8 percent) of the patients with single complex plaques; it was not performed in the other 8 patients (5.2 percent) because of the presence of technically unsuitable vessels. Angioplasty was successful in 97.9 percent of the patients in whom it was performed. Urgent bypass surgery was performed because of severe multivessel disease in eight (5.2 percent) of the patients with single complex plaques. No patients with single complex plaques underwent initial multivessel angioplasty, but 15 patients with sin-

TABLE 1. CLINICAL OUTCOMES OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND SINGLE OR MULTIPLE COMPLEX CORONARY PLAQUES.*

OUTCOME	SINGLE PLAQUE (N=153)	MULTIPLE PLAQUES (N=100)	P VALUE
During hospitalization			
Multivessel disease ($\geq 50\%$ stenosis) — no. (%)	114 (74.5)	91 (91.0)	≤ 0.001
Left ventricular ejection fraction — %	45 \pm 14	38 \pm 14	0.003
Initial primary PTCA — no. (%)	145 (94.8)	86 (86.0)	0.03
Initial multivessel PTCA — no. (%)	0	13 (13.0)	0.003
Initial urgent CABG — no. (%)	8 (5.2)	27 (27.0)	≤ 0.001
Planned staged PTCA — no. (%)	15 (9.8)	20 (20.0)	0.03
After discharge			
Repeated catheterization within 6 mo — no. (%)	22 (14.4)	39 (39.0)	≤ 0.001
Repeated catheterization within 1 yr — no. (%)	37 (24.2)	54 (54.0)	≤ 0.001
Recurrent acute coronary syndromes within 1 yr — no. (%)	4 (2.6)	19 (19.0)	≤ 0.001
Repeated PTCA within 1 yr — no. (%)	19 (12.4)	32 (32.0)	≤ 0.001
PTCA of infarct-related lesion — no. (%)	12 (7.8)	15 (15.0)	0.07
PTCA of non-infarct-related lesion — no. (%)	7 (4.6)	17 (17.0)	≤ 0.001
CABG within 1 yr — no. (%)	17 (11.1)	35 (35.0)	≤ 0.001
Death			
In hospital — no. (%)	12 (7.8)	11 (11.0)	0.30
Cumulative, within 1 yr — no. (%)	19 (12.4)	17 (17.0)	0.32

*Plus-minus values are means \pm SD. PTCA denotes percutaneous transluminal coronary angioplasty, and CABG coronary-artery bypass grafting.

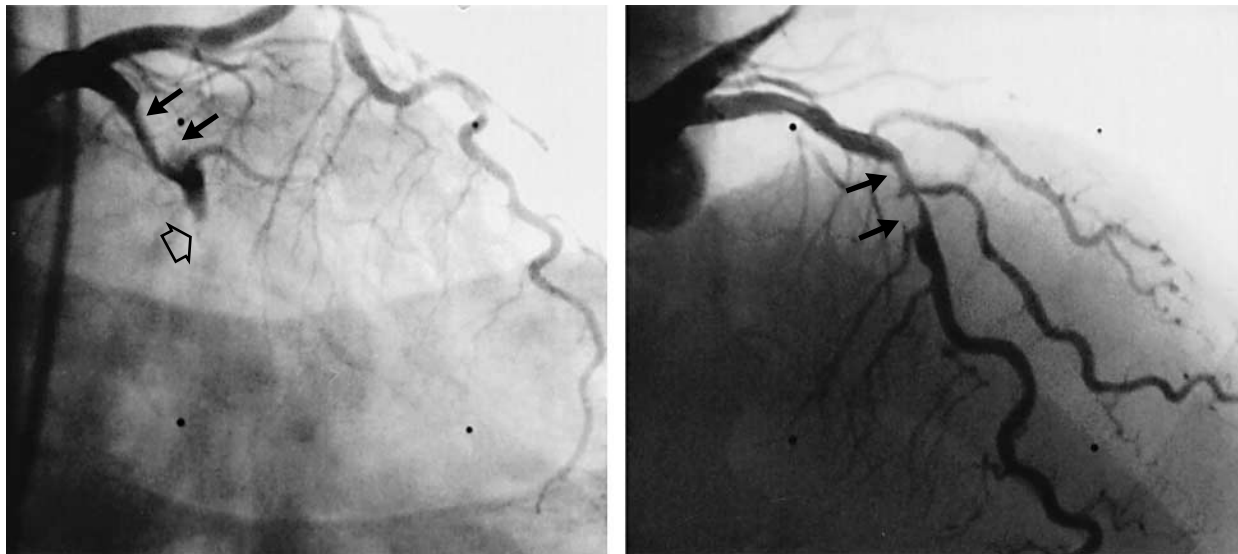


Figure 1. Angiograms from a Patient with Acute Posterolateral Myocardial Infarction.

The left-hand panel shows a culprit lesion in the circumflex artery, characterized by a long, scalloped, ulcerated, tight stenosis with haziness and ulceration (solid arrows) and with a total occlusion located just distally (open arrow). The right-hand panel shows a cranial view of the left anterior descending coronary artery in the same patient, demonstrating a complex ulcerated stenosis with overhanging edges (arrows), anatomically remote from the culprit occlusion in the circumflex artery.

gle complex plaques (9.8 percent) underwent planned staged percutaneous interventions for lesions in vessels other than the primary infarct-related artery.

In contrast, patients with multiple complex plaques were less likely than those with single complex plaques to undergo initial angioplasty of the infarct-related lesion (86.0 percent vs. 94.8 percent, $P=0.03$) (Table

1). Not surprisingly, such patients required urgent bypass surgery more frequently than those with single complex plaques (27.0 percent vs. 5.2 percent, $P\leq 0.001$). Patients with multiple complex plaques more commonly underwent initial emergency multivessel percutaneous interventions (13.0 percent vs. 0 percent, $P=0.003$), as well as planned staged angio-

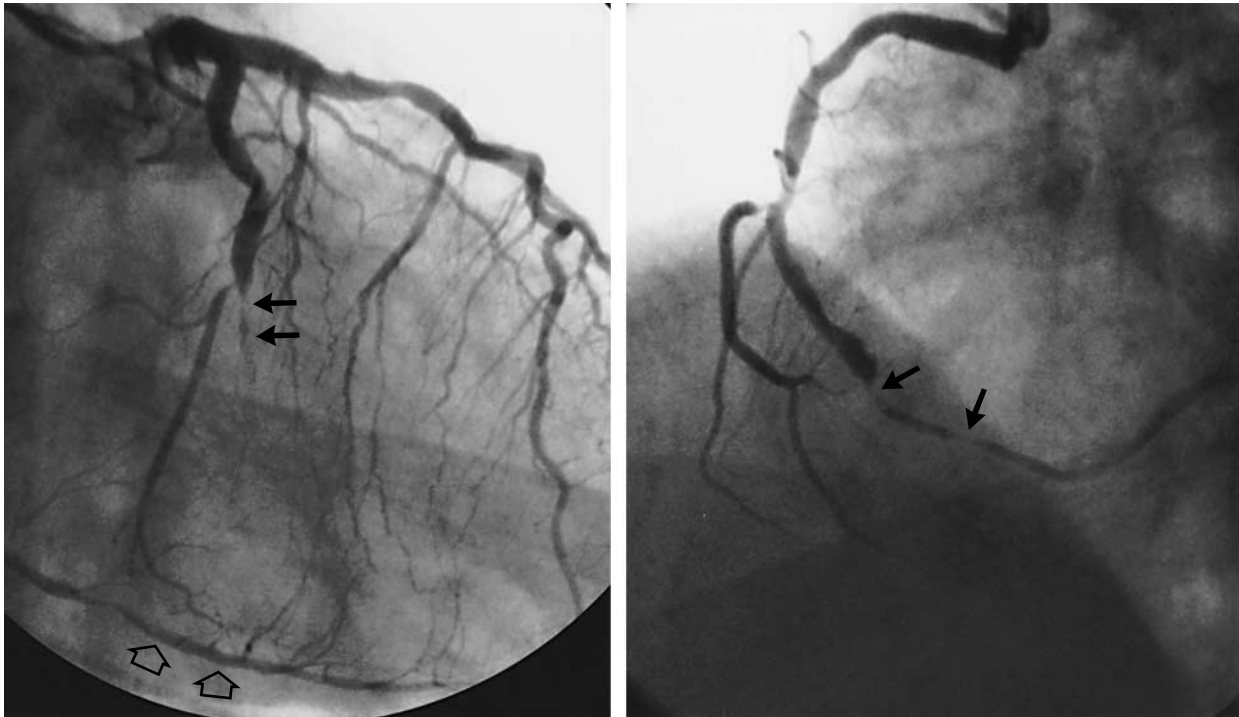


Figure 2. Angiograms from a Patient with Acute Inferior–Posterior Myocardial Infarction.

Angiography of the left coronary artery (left-hand panel) shows acute occlusion of the circumflex artery (solid arrows), with haziness, a filling defect, and impaired flow consistent with the presence of an acute thrombotic occlusion. Collateral filling of the distal right coronary artery is evident (open arrows). Angiography of the right coronary artery in the same patient (right-hand panel) demonstrates near-total distal occlusion (arrows), with abrupt cutoff, haziness, and a filling defect consistent with acute thrombosis.

plasty (20.0 percent vs. 9.8 percent, $P=0.03$). However, the success of primary angioplasty was not significantly different in patients with single and those with multiple complex plaques. In-hospital mortality was slightly higher among those with multiple complex plaques (11.0 percent vs. 7.8 percent, $P=0.30$).

Outcome within One Year

Ninety-three percent of all patients were followed for one year after myocardial infarction (95 percent of those with single and 90 percent of those with multiple complex plaques, P not significant). Among those with single complex plaques, recurrent ischemia requiring repeated catheterization developed in 22 patients (14.4 percent) within 6 months and in 37 patients (24.2 percent) within 12 months, with recurrent acute coronary syndromes in 4 patients (2.6 percent) (Table 1 and Fig. 3). Nineteen patients (12.4 percent) underwent repeated angioplasty: 12 (7.8 percent) in the infarct-related lesion and 7 (4.6 percent) in another lesion. Coronary bypass surgery was necessary in 17 patients (11.1 percent).

As compared with patients with single complex plaques, those with multiple complex plaques were more likely to have recurrent ischemia requiring re-

peated catheterization by six months (39.0 percent vs. 14.4 percent, $P\leq 0.001$) and by one year (54.0 percent vs. 24.2 percent, $P\leq 0.001$) and also had a higher incidence of recurrent acute coronary syndromes (19.0 percent vs. 2.6 percent, $P\leq 0.001$) (Tables 1 and 2 and Fig. 3). Within one year of the original myocardial infarction, patients with multiple complex plaques were more likely than those with single complex plaques to require repeated angioplasty of any lesion (32.0 percent vs. 12.4 percent, $P\leq 0.001$) or of a lesion other than the infarct-related plaque (17.0 percent vs. 4.6 percent, $P\leq 0.001$). Repeated angioplasty was performed on a previously documented complex plaque in 15 of the 17 patients with multiple complex plaques who underwent angioplasty on a non–infarct-related lesion (88.2 percent); 13 of these 17 patients (76.5 percent) presented with recurrent acute coronary syndromes. Furthermore, patients with multiple complex plaques were more likely to require coronary bypass surgery than those with single complex plaques (35.0 percent vs. 11.1 percent, $P\leq 0.001$). Those with multiple complex plaques had a slightly higher mortality rate during the year after infarction (17.0 percent vs. 12.4 percent, $P=0.32$).

Multivariate analysis showed that the presence of

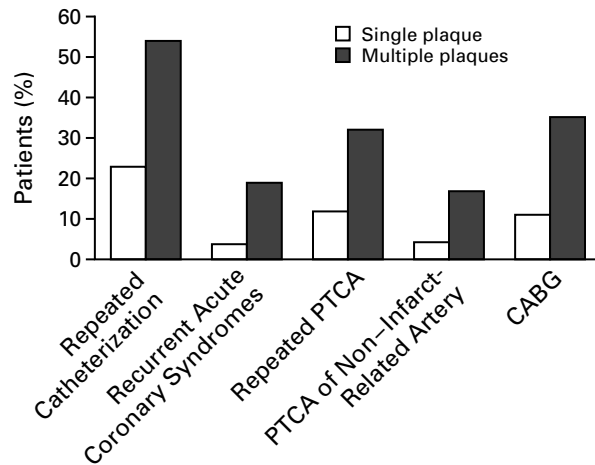


Figure 3. Outcomes within One Year after Myocardial Infarction in Patients with Multiple Complex Plaques or Single Complex Plaques.

PTCA denotes percutaneous transluminal coronary angioplasty, and CABG coronary-artery bypass grafting. $P \leq 0.001$ for all comparisons between groups.

multiple complex plaques was independently predictive of adverse outcomes (Table 2). For recurrent acute coronary syndromes, repeated catheterization, or bypass surgery within one year, only the presence of multiple complex plaques was found to be a significant predictor. For repeated angioplasty, the presence of multiple complex plaques and an age of 70 years or more were significant predictors. The presence of multiple complex plaques was a significant predictor of

multiple adverse cardiac events, as was a lower left ventricular ejection fraction.

Analysis of Patients with Multivessel Disease

Since the initial revascularization strategies and the rates of recurrent ischemia and revascularization over time might be expected to differ between patients with multivessel disease and those with single-vessel disease, independently of the presence or absence of multiple complex plaques, a separate analysis of patients with multivessel disease was performed. Multivessel disease was common in patients with single complex plaques (74.5 percent); not surprisingly, it was even more prevalent in those with multiple complex plaques (91.0 percent, $P \leq 0.001$). Patients with multivessel disease and multiple complex plaques were less likely than those with multivessel disease and single complex plaques to undergo initial primary angioplasty (86.0 percent vs. 93.2 percent, $P = 0.03$) and more commonly required urgent primary coronary bypass surgery initially (25.0 percent vs. 4.1 percent, $P \leq 0.001$). Within a year after infarction, as compared with patients with single complex plaques, patients with multiple complex plaques had a higher incidence of recurrent ischemia requiring repeated catheterization (56.0 percent vs. 25.6 percent, $P \leq 0.001$), recurrent acute coronary syndromes (1.3 percent vs. 19.0 percent, $P \leq 0.001$), subsequent revascularization (32.0 percent vs. 14.4 percent [$P = 0.002$] for any angioplasty; 16.0 percent vs. 6.3 percent [$P = 0.02$] for angioplasty of a lesion other than the initial culprit lesion), and coronary bypass surgery (33.0 percent vs. 11.7 percent, $P \leq 0.001$). There was no significant difference in mortality at one year (16.0 percent vs. 14.3 percent, P not significant).

TABLE 2. STEP-DOWN MULTIVARIATE ANALYSIS OF OUTCOMES WITHIN ONE YEAR AFTER ACUTE MYOCARDIAL INFARCTION.*

OUTCOME	COVARIATE	ODDS RATIO (95% CI)	P VALUE
Recurrent acute coronary syndromes	Multiple complex plaques	10.6 (3.5–31.9)	<0.001
	Age ≥ 70 yr		0.39
	Male sex		0.86
Repeated catheterization	Multiple complex plaques	3.2 (1.8–5.6)	<0.001
	Age ≥ 70 yr		0.16
	Male sex		0.19
Repeated PTCA	Multiple complex plaques	2.8 (1.4–5.6)	0.003
	Age ≥ 70 yr	0.96 (0.93–0.99)	0.008
	Male sex		0.48
CABG within 1 yr	Multiple complex plaques	4.3 (2.2–8.3)	<0.001
	Age ≥ 70 yr		0.21
	Male sex		0.07
Multiple adverse cardiac events	Multiple complex plaques	6.8 (3.2–14.4)	<0.001
	Age ≥ 70 yr		0.33
	Male sex		0.35
	Left ventricular ejection fraction $\leq 40\%$	0.98 (0.95–1.00)	0.05

*CI denotes confidence interval, PTCA percutaneous transluminal coronary angioplasty, and CABG coronary-artery bypass grafting.

DISCUSSION

The results of this study demonstrate that patients with acute myocardial infarction may harbor multiple complex coronary plaques, which are associated with adverse clinical outcomes. These observations support the concept that plaque instability is not merely a local vascular accident but probably reflects more generalized pathophysiologic processes with the potential to destabilize atherosclerotic plaques throughout the coronary tree.

In the present study, two fifths of the patients had angiographic evidence of multiple complex coronary plaques, which were associated with a less favorable in-hospital course. Patients with multiple complex plaques were less likely to undergo primary angioplasty, were more likely to require early coronary-artery bypass surgery or staged multivessel angioplasty, and had greater depression of left ventricular function than those with single complex plaques. The presence of multiple complex plaques was independently predictive of clinical events. Patients with multiple complex plaques had a more complicated course during the year after myocardial infarction. They had a higher incidence of recurrent angina and acute coronary syndromes. They were more likely to require repeated angioplasty, which could be directed not only at the initial culprit plaque but also at non-infarct-related plaques previously identified as complex. They were also more likely to require coronary-artery bypass surgery.

Our angiographic findings document the presence of multiple complex coronary plaques and their influence on outcome in patients with acute transmural myocardial infarction. However, similar multifocal plaque instability is evident in previous pathological studies of patients with acute ischemic heart disease.^{1,2,16-20} Multiple coronary thrombi were identified in an autopsy study of 100 patients who died within six hours of acute myocardial infarction, with 115 separate thrombi found in 74 patients.² Multiple coronary thrombi and multicentric plaque rupture have been found in other autopsy studies of fatal acute ischemic heart disease.^{1,16-20}

The presence of coronary plaques with complex morphologic features is the angiographic hallmark of unstable coronary syndromes^{14,15,21-32} and correlates with pathologic plaque rupture and thrombus.^{21,23,24} Progression of stenosis and clinical instability are characteristic of such lesions.²⁴⁻³¹ As in the present study, multiple complex plaques have been documented by angiography in patients with unstable angina (at an average of 2.6 complex plaques per patient)³² and in patients with nontransmural infarction (423 complex lesions in 274 patients).³³ The concept of multifocal plaque instability is also supported by angiographic natural-history studies in patients with acute myocardial infarction,²² in whom rapid progression of both culprit and nonculprit lesions over a period of one

month has been documented. Angiographic natural-history studies in patients with unstable angina similarly demonstrate rapid progression not only of the initial culprit lesion, but also of nonculprit complex lesions.^{24,25} As in the present study, prior reports demonstrate that stenoses caused by angiographically detectable complex plaques are associated with a poor prognosis,^{23,24} with a striking association between complex morphologic features and clinical instability.²²⁻³¹ However, in some cases, complex plaques may remain stable over time.³⁴

The present findings may have implications regarding the pathophysiology of plaque instability. Weakening and disruption of its protective fibrous cap appear to be the critical events triggering plaque instability.³⁻⁵ Autopsy and atherectomy specimens document that, as compared with stable plaques in the same patient, unstable plaques are characterized by active inflammation of the fibrous cap, concentrated at the point of plaque disruption.^{8,9} Inflammatory cells may activate matrix metalloproteinases that degrade the extracellular matrix and thereby weaken the fibrous cap.^{35,36} Inflammation of the fibrous cap, whether related to the toxic effects of oxidized low-density lipoproteins, viral triggers, or other factors,¹⁻⁵ may arise from systemic processes and thereby affect the atherosclerotic coronary vasculature in a more diffuse pattern.

Intrinsic plaque instability may develop owing to the expansion of intraplaque contents (e.g., lipid-pool swelling),¹⁻⁶ which may also reflect systemic derangements in lipid metabolism. Intraluminal mechanical forces implicated as extrinsic triggers of plaque rupture are also fundamentally influenced by determinants that exert effects throughout the coronary tree.^{10,11} Systemic alterations in platelet aggregability and clotting factors implicated in triggering acute myocardial infarction³⁷ would also be expected to increase the thrombogenic potential of vulnerable eroded plaques throughout the coronary vessels.

Clinical observations support the concept that systemic processes influence plaque instability. Patients with acute myocardial infarction have evidence of systemic inflammation, as reflected by elevated levels of C-reactive and amyloid proteins.³⁸⁻⁴⁰ Elevation of serologic markers of macrophage activity has been correlated with the presence of multiple complex plaques in patients with unstable angina.³² The cardioprotective benefits of aspirin against recurrent myocardial infarction may be mediated in part by its systemic antiinflammatory effects.³⁹ The reduction in recurrent myocardial infarction produced by systemic lipid-lowering interventions designed to stabilize plaques adds further support to the notion that unstable coronary artery disease is a multifocal process influenced by systemic factors.⁴⁰ In aggregate, these pathological, angiographic, and clinical observations support the concept that, at least in some patients, acute coronary artery disease reflects a diffuse

pathophysiologic process that may lead to multifocal plaque instability and rapid plaque progression associated with clinical instability.

It is important to emphasize the limitations of this study. The retrospective nature of the analysis could have influenced the results. Angiography has a limited ability to delineate the severity and complexity of coronary disease and to determine whether a given complex lesion is acute or chronic. Complex-lesion morphology may in some cases reflect more chronic occlusions; conversely, subtler plaque ulcerations may not be angiographically apparent. Although angiographically determined complexity correlates closely with plaque instability pathologically,²¹ and although complex plaques are associated with angiographic progression and clinical instability,²⁴⁻³¹ such plaques may remain stable over time³⁴; therefore angiographic evidence of complexity does not by itself necessarily determine the destiny of a plaque.

The present observations may have implications regarding the natural history and management of acute coronary syndromes. Our results demonstrate that the presence of multiple complex coronary plaques on angiography identifies a subgroup of patients at increased risk for recurrent ischemia, even after successful initial acute percutaneous interventions. The next step will be to determine whether strategies designed to stabilize plaques by pharmacologic interventions (e.g., by aggressive lipid lowering or the use of antiinflammatory drugs) or multilesion revascularization by percutaneous or surgical methods would be beneficial in patients with multiple complex coronary plaques.

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