JACC Vol. 27, No. 7
June 1996:1662–8

Influence of Cigarette Smoking on Rate of Reopening of the Infarct-Related Coronary Artery After Myocardial Infarction: A Multivariate Analysis

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Objectives. **This study sought to determine whether the reopening of the infarct-related vessel is related to clinical characteristics or cardiovascular risk factors, or both.**

Background. **In acute myocardial infarction, thrombolytic therapy reduces mortality by restoring the patency of the infarct-related vessel. However, despite the use of thrombolytic agents, the infarct-related vessel remains occluded in up to 40% of patients.**

Methods. **We studied 295 consecutive patients with an acute myocardial infarction who underwent coronary angiography within 15 days (mean [±SD] 6.7 ± 3.2 days) of the onset of symptoms. Infarct-related artery patency was defined by Thrombolysis in Myocardial Infarction trial flow grade ≥2. Four cardiovascular risk factors—smoking, hypertension, hypercholesterolemia and diabetes mellitus—and eight different variables—age, gender, in-hospital death, history of previous myocardial infarction, location of current myocardial infarction, use of thrombolytic agents, time interval between onset of symptoms, thrombolytic therapy and coronary angiography—were recorded in all patients.**

Results. **Thrombolysis in current smokers and anterior infarct location on admission were the three independent factors highly correlated with the patency of the infarct-related vessel (odds ratios 3.2, 3.0 and 1.9, respectively). In smokers, thrombolytic therapy was associated with a higher reopening rate of the infarct vessel, from 35% to 77% ($p < 0.001$). Nonsmokers did not benefit from thrombolytic therapy, regardless of infarct location.**

Conclusions. **These observational data, if replicated, suggest that in patients with acute myocardial infarction, thrombolytic therapy may be most effective in current smokers, whereas nonsmokers and ex-smokers may require other management strategies, such as emergency percutaneous transluminal coronary angioplasty.**

(J Am Coll Cardiol 1996;27:1662–8)

Large studies have established that in patients with acute myocardial infarction, thrombolysis reduces mortality (1–5), with a reduction in infarct size (6,7), thus preserving left ventricular function.

The rationale for the use of thrombolytic agents in the management of an acute myocardial infarction is derived from angiographic studies from the early 1980s (8,9), demonstrating total coronary obstruction in the early course of a myocardial infarction in a large percentage of patients. These studies also demonstrated the ability of thrombolytic agents to reopen the infarct-related coronary vessel, supporting the hypothesis that the occlusion is mostly due to a thrombus.

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Manuscript received April 27, 1995; revised manuscript received January 31, 1996, accepted February 27, 1996.

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However, despite the use of thrombolytic agents in the acute phase of a myocardial infarction, the infarct-related coronary artery remains occluded in up to 40% of cases (10).

In the present study, we investigated the hypothesis that in patients treated with thrombolytic agents in the early phase of a myocardial infarction, the absence of reopening of the infarct-related coronary vessel may be related to some clinical characteristics or to cardiovascular risk factors.

Methods

Patients (Fig. 1). Of 368 patients referred to three university-affiliated coronary care units for an acute myocardial infarction during a 1-year period, 295 underwent elective cardiac catheterization within 15 days of the onset of symptoms and were included in the present observational study, which was not a randomized trial. The remaining 73 patients did not undergo coronary angiography and so were excluded from the study. In these 73 patients, coronary angiography was not performed for the following reasons: 1) death in the early phase of the myocardial infarction (n = 25) before coronary

0735-1097/96/$15.00
PII S0735-1097(96)00091-5

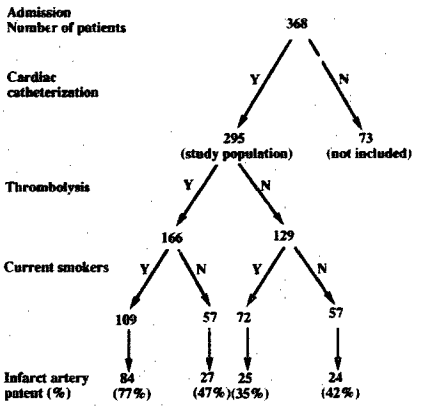

Figure 1. Diagram showing classification of patients after hospital admission according to cardiac catheterization, smoking status, thrombolytic therapy and patent arteries. For convenience, nonsmokers and ex-smokers were combined. Y = yes; N = no.

angiography was performed; 2) age ≥80 years (n = 18); 3) poor patient condition owing to associated noncardiac disease (n = 25); and 4) refusal to give informed consent for cardiac catheterization (n = 5).

In the 295 catheterized patients, the specific indications for cardiac catheterization were 1) cardiogenic shock (n = 8); 2) urgent angiography for ongoing angina since the onset of the infarction (n = 47); 3) recurrent angina (n = 38); and 4) systematic angiographic evaluation after the infarction (n = 202). The first three indications correspond to acute complications of the myocardial infarction, leading to earlier cardiac catheterization as compared with systematic angiography (1.9 ± 3.0 days vs. 7.3 ± 2.6 days; $p < 0.001$).

In the study group, 166 (56%) of the 295 patients admitted within 6 h of the onset of symptoms received intravenous thrombolytic therapy, either streptokinase (n = 85, 1.5 million U over 60 min) or recombinant tissue-type plasminogen activator (rt-PA) (n = 81, 15-mg bolus followed by an infusion of 0.75 mg/kg body weight over 30 min [maximum 50 mg] and then an infusion of 0.50 mg/kg over 60 min [maximum 35 mg]). The allocation of streptokinase or rt-PA was not randomized and was only based on the decision of the physician who prescribed the treatment.

The remaining 129 (44%) patients did not receive thrombolytic therapy because of a long delay (>6 h) between the onset of symptoms and hospital admission (n = 105) or a contraindication to thrombolytic therapy—primary ventricular fibrillation necessitating resuscitation at the onset of the infarction (n = 4), history of gastric ulcer or digestive bleeding (n = 11), history of cerebral stroke (n = 5) or a recent operation (n = 4).

In all patients, intravenous heparin was introduced on admission with a bolus of 5,000 IU followed by a constant infusion of 1,000 IU/h, adjusted as needed to maintain an activated partial thromboplastin time of 90 to 110 s. On day 5, intravenous heparin was replaced by subcutaneous heparin with the same daily dosage. Aspirin was routinely administered within 24 h of admission with an oral daily dose of 250 mg.

Variables Assessed

Cardiovascular risk factors. Risk factors for myocardial infarction were assessed by a structured questionnaire administered by a physician. In total, four risk factors were evaluated, as discussed next.

Smoking status. Based on the information obtained, patients were classified as current smokers, nonsmokers and ex-smokers. Current smokers were patients with a consumption of tobacco at the time of entry into the hospital, and nonsmokers consisted of patients who had never smoked. Based on the results of the questionnaire, all ex-smokers had abstained from smoking for at least 1 year before admission for the current infarction. Lifetime tobacco use was calculated as the total number of years of smoking multiplied by the average number of cigarettes smoked per day, divided by 20, and expressed as pack-years of smoking.

Diabetes mellitus. A patient was defined as having diabetes if a physician diagnosed diabetes before or at the time of the current myocardial infarction.

Hypertension. Hypertension was defined by history of several blood pressure measurements elevated either systolically (>160 mm Hg) or diastolically (>95 mm Hg).

Hypercholesterolemia. Hypercholesterolemia was defined by an elevated total serum cholesterol level of 6.2 mmol/liters, measured before or at the time of the current myocardial infarction (11).

Clinical characteristics. Apart from the questionnaire on cardiovascular risk factors, eight variables were systematically registered in all patients: 1) age, 2) gender, 3) history of a previous myocardial infarction, 4) location of the present myocardial infarction, 5) use of thrombolytic therapy in the early phase of the present myocardial infarction, 6) time interval between the onset of symptoms and thrombolytic therapy (when appropriate), 7) time interval between the onset of symptoms and coronary angiography, and 8) occurrence and cause of death during the hospital stay.

Coronary angiography. Cardiac catheterization was performed between 12 h and 15 days after the onset of symptoms (mean [±SD] 5.6 ± 3.7 days).

The coronary angiograms were analyzed by two experienced physicians who had no knowledge of the patients' clinical characteristics and cardiovascular risk factors, the time interval between admission and therapy and the clinical outcome. Angiographic data included five variables: 1) the number of coronary artery diseased vessels, as defined by the Coronary Artery Surgery Study (12); 2) the infarct-related coronary artery; 3) the patency status of the infarct-related coronary artery; 4) the residual stenosis severity of the infarct-related vessel, when appropriate; and 5) the value of the left ventricular ejection fraction, calculated by a computer accord-

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ing to the area–length method from a cineangiogram in the 30° right anterior oblique view.

The infarct-related coronary artery was identified by electrocardiography on hospital admission, ventriculographic contraction abnormalities and angiographic findings. The patency status of the infarct-related coronary artery was evaluated using the grading of the Thrombolysis in Myocardial Infarction (TIMI) trial (5). A patent vessel was defined by a TIMI flow grade ≥2.

Statistical analysis. Patients were classified in two outcome groups: the patent artery group included patients with a patent infarct-related coronary artery, and the occluded artery group included patients with an occluded infarct-related coronary vessel.

Statistical analysis was performed with a BMDP program (BMDP Statistical Software, Inc.) on an IBM 486/66 microcomputer.

Univariate logistic regression analysis was first performed with each variable to determine which ones were significantly related to the presence of a patent vessel. For multivariate analysis, the significant variables were entered in the logistic regression equation in a stepwise fashion based on the maximal likelihood ratio: the first variable entered was the one that gave the best improvement of the chi-square test, and so on, for the following variables, given that all previously entered variables remained in the equation. The odds ratio (OR) was estimated for each variable found to be correlated with the presence of a patent infarct-related coronary artery.

In addition, the statistical interaction was studied to determine the influence of each variable on the different relations found to be significant by statistical analysis.

Continuous variables are expressed as mean value ± SD. Statistical significance was defined as $p < 0.05$.

Results

Clinical data. The study group included 295 patients (239 men, 56 women [gender ratio 4.27]; mean age 59 ± 12 years, range 27 to 79). Of 295 patients, 181 (61%) were smokers, 93 (32%) were nonsmokers and 21 (7%) were ex-smokers. Ex-smokers had quit smoking for 12.1 ± 8.8 years on average (range 1 to 35). Average tobacco consumption was 33.4 ± 12.4 pack-years of smoking (range 10 to 90) in current smokers and 26.4 ± 11.8 pack-years of smoking (range 5 to 50) in ex-smokers ($p = 0.01$).

A history of hypertension was found in 93 (32%) patients; hypercholesterolemia was present in 103 (35%) patients; and diabetes mellitus was present in 23 (8%) patients. Forty (14%) patients had a history of a previous myocardial infarction. Because all of them underwent coronary angiography within 15 days of the first infarction, the coronary vessel responsible for the current infarction could be easily determined by comparing the two angiograms, when necessary.

The current myocardial infarction was anterior in 134 (45%) patients and inferior in 161 (55%) patients.

Thrombolytic therapy was used in the acute phase of the current myocardial infarction in 166 (56%) patients, with a mean delay of 3.1 ± 1.2 h since the onset of symptoms (range 0.5 to 6).

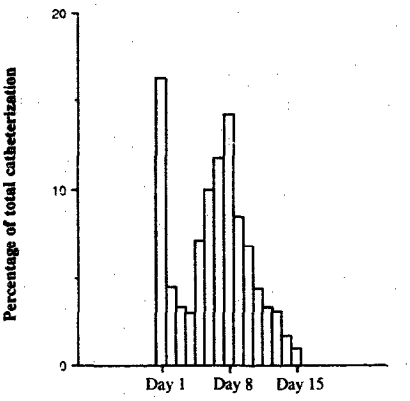

Figure 2. Histogram showing frequency of cardiac catheterizations versus time interval from onset of myocardial infarction.

Among the 295 patients, 11 died before hospital discharge (cardiogenic shock [n = 5], left free wall rupture [n = 4] and postoperative complication after emergency coronary artery bypass grafting [n = 2]).

Angiographic data. Coronary angiography was performed between 12 h and 15 days after the onset of symptoms (mean 5.6 ± 3.7 days). Figure 2 shows a histogram of the frequency of coronary angiograms versus the time interval from the onset of the myocardial infarction. Ninety-three (31.5%) of the 295 patients underwent cardiac catheterization for cardiogenic shock (n = 8), persistent chest pain since the onset of symptoms (n = 47) or recurrence of clinical myocardial ischemia (n = 38). In these 93 patients, the time interval between the onset of symptoms and cardiac catheterization was shorter (1.9 ± 3.0 days vs. 7.3 ± 2.6 days; $p < 0.001$) than that in the remaining 202 patients, in whom catheterization was performed in the absence of acute complications in the early course of the infarction.

The infarct-related vessel was the left anterior descending artery in 116 (39%) patients, the circumflex artery in 56 (19%) patients and the right coronary artery in 123 (42%) patients. The infarct artery was completely occluded (TIMI flow grade 0) in 106 (36%) patients. The distribution of the other TIMI flow grades was grade 1 in 29 (10%) patients, grade 2 in 57 (19%) patients and grade 3 in 103 (35%) patients. Single-vessel disease was found in 143 (48.5%) patients, whereas 83 (28%) patients had two-vessel disease and 69 (23.5%) patients had three-vessel disease.

The mean (±SD) value of the left ventricular ejection fraction was 0.51 ± 0.12 (range 0.13 to 0.75). Only two factors were associated with a higher value for the left ventricular ejection fraction: an inferior wall myocardial infarction (0.54 ± 0.10 vs. 0.48 ± 0.14; $p < 0.001$) and reopening of the

Table 1. Relation Between Patency Status of Infarct-Related Vessel and Cardiovascular Risk Factors and Coagulation Variables

	Patent Artery (TIMI 2 or 3) (n = 160)	Occluded Artery (TIMI 0 or 1) (n = 135)	p Value
Diabetes	9 (6%)	14 (10%)	0.20
Hypertension	39 (24%)	31 (23%)	0.88
HCT	59 (37%)	44 (33%)	0.52
Smoking status			
Smokers	109 (68%)	72 (53%)	< 0.01
PYS	31.9 ± 12.6	35.6 ± 13.3	0.06
Nonsmokers	42 (26%)	51 (38%)	< 0.05
Ex-smokers	9 (6%)	12 (9%)	0.39
PYS	28.9 ± 12.4	24.6 ± 11.6	0.42
Fibrinogen (g/dl)	3.58 ± 1.28	3.78 ± 1.42	0.22
Hematocrit (%)	0.41 ± 0.03	0.41 ± 0.03	0.97
Platelets ($\times 10^9$/liter)	258 ± 68	249 ± 66	0.25

Data presented are mean value ± SD or number (%) of patients. HCT = hypercholesterolemia; PYS = pack-years of smoking (when applicable); TIMI = Thrombolysis in Myocardial Infarction flow grade.

Table 2. Relation Between Patency Status of Infarct-Related Vessel and Clinical and Biologic Data

	Patent Artery (TIMI 2 or 3) (n = 160)	Occluded Artery (TIMI 0 or 1) (n = 135)	p Value
Age (yr)	57.5 ± 12.1	61.3 ± 11.6	< 0.01
Men	128 (80%)	111 (82%)	0.74
Previous MI	16 (10%)	24 (18%)	0.08
Anterior wall MI	82 (51%)	52 (39%)	< 0.05
Thrombolysis	111 (69%)	55 (41%)	< 0.001
S-Thromb. (h)	3.4 ± 1.9	3.2 ± 1.2	0.29
S-CA (days)	6.7 ± 2.8	6.7 ± 3.6	1.00
In-hospital death	2 (1%)	9 (7%)	< 0.05

Data presented are mean value ± SD or number (%) of patients. MI = myocardial infarction; S-CA = delay between symptoms and coronary angiography; S-Thromb. = delay between symptoms and thrombolysis; TIMI = Thrombolysis in Myocardial Infarction flow grade.

infarct-related vessel (0.54 ± 0.11 vs. 0.48 ± 0.12; $p < 0.001$). The use of thrombolytic therapy was not correlated, per se, with the value of the left ventricular ejection fraction (0.52 ± 0.12 vs. 0.51 ± 0.12, respectively, for thrombolysis and absence of thrombolysis).

Univariate analysis. *Infarct-related coronary artery patency status in relation to cardiovascular risk factors and coagulation variables.* As shown in Table 1, there was no relation between diabetes mellitus, a history of hypertension or hypercholesterolemia and the patency status of the infarct-related vessel. We did not observe any relation between fibrinogen level, platelets count or hematocrit and the patency status of the infarct-related vessel.

There was a relation between smoking status and patency of the infarct-related vessel: The percentage of smokers was higher in patients with a patent vessel than patients with an occluded vessel.

The infarct-related artery patency rate was 60% in smokers (109 of 181), 45% in nonsmokers (42 of 93) and 43% in ex-smokers (9 of 21) ($p = 0.03$).

Infarct-related coronary artery patency status in relation to clinical data. As shown in Table 2, no correlation was found between the patency status of the infarct-related vessel and gender, history of previous myocardial infarction, time interval between the onset of symptoms and thrombolytic therapy or the time interval between the onset of symptoms and coronary angiography.

The rate of infarct-related vessel reopening was similar in patients who received streptokinase (61 of 85 [72%]) as compared with those treated with rt-PA (50 of 81 [62%]).

Patients with a patent infarct-related vessel were younger than patients with an occluded vessel (57.5 ± 12.1 years vs. 61.3 ± 11.6 years, respectively; $p < 0.01$), and the percentage of anterior wall myocardial infarction was higher in the patent artery group than in the occluded artery group (51% vs. 39%, respectively; $p < 0.05$). As expected, the percentage of thrombolysis was higher in patients with a patent infarct-related vessel as compared with patients with an occluded vessel (69% vs. 41%, respectively; $p < 0.01$).

Eleven patients died during their hospital stay. Death occurred more frequently in the occluded artery group than in the patent artery group (7% vs. 1%; $p < 0.05$).

Infarct-related coronary artery patency status in relation to smoking status and thrombolysis (Table 3). In patients who did not receive thrombolytic therapy, the rates of reopening of the infarct-related vessel were similar in smokers, nonsmokers and ex-smokers (35%, 42% and 43%, respectively). In nonsmokers and ex-smokers, the rate of infarct-related artery patency was independent of the treatment received (thrombolytic therapy or not). Smokers treated with thrombolytic therapy had a higher rate of reopening of the infarct-related vessel as compared with smokers not treated with thrombolytic agents (OR 2.2), as well as non- or ex-smokers treated with thrombolytic agents (OR 1.6). Similar results were observed when the

Table 3. Relation Between Smoking Status, Thrombolysis and Patency of the Infarct-Related Vessel

	Thrombolysis (n = 166)	No Thrombolysis (n = 129)	p Value
IRCA patency			
Smokers	84/109 (77%)	25/72 (35%)	< 0.001
Nonsmokers	21/43 (49%)	21/50 (42%)	0.65
Ex-smokers	6/14 (43%)	3/7 (43%)	0.64
p value	< 0.001	0.69	
IRCA: TIMI flow grade 3 only			
Smokers	53/109 (49%)	19/72 (26%)	< 0.005
Nonsmokers	12/43 (28%)	15/50 (30%)	0.99
Ex-smokers	3/14 (21%)	1/7 (14%)	0.84
p value	< 0.02	0.67	

Data presented are number (%) of patients. IRCA = infarct-related coronary artery; TIMI = Thrombolysis in Myocardial Infarction.

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definition of coronary artery patency was defined only as TIMI flow grade 3.

Early reperfusion in relation to smoking status and thrombolysis. Forty-eight (16.3%) of the 295 patients underwent cardiac catheterization within 24 h of the onset of symptoms. In these patients, the reasons to perform early catheterization were 1) persistence of chest pain, although decreased since admission, possibly related to an absence of reperfusion of the infarct-related vessel (n = 41); 2) recurrent chest pain associated with ST segment modifications (n = 2); and 3) cardiogenic shock (n = 5).

Of these 48 patients, 28 (58%) were current smokers. Of these 28, 23 (82%) received thrombolytic therapy in the early phase of the infarction and the rate of infarct-related artery patency was 70% (16 of 23). Of the remaining 20 nonsmokers, 12 (60%) were treated with thrombolytic agents and only 2 (17%) of the 12 subsequently had a patent infarct-related vessel (p = 0.009 as compared with smokers).

Multivariate analysis. Multivariate analysis showed that three of the four factors identified by univariate analysis were independent (thrombolysis, infarct location and smoking status). The odds ratio of having a patent infarct-related vessel was multiplied by 3.2, 3.0 and 1.9, respectively, for the use of thrombolytic therapy, the anterior location of the myocardial infarction and current consumption of tobacco on the day of admission.

When an interaction was identified between any two variables in the univariate analysis, this interaction was entered in the multivariate analysis model. Hence, the multivariate analysis took confounding variables into account to determine the independent variables associated with the patency of the infarct-related vessel.

Comparison of clinical data and nonclinical variables in relation to smoking status. There was no relation between history of previous myocardial infarction, current infarct location, diabetes mellitus, history of hypertension or hypercholesterolemia and the smoking status on admission. Neither did we observe relation between fibrinogen level, platelets count or hematocrit and the smoking status on admission.

Smokers were younger (56.2 ± 11.9 years vs. 64.7 ± 10.5 years; p < 0.001), were predominantly men (85% vs. 68%; p < 0.001) and received thrombolytic therapy more frequently as compared with nonsmokers (60% vs. 46%; p = 0.04). There was a relation between the smoking status and the patency status of the infarct-related vessel, the reopening of the infarct vessel being higher in smokers (60% vs. 45%; p = 0.025). No correlation was found between the number of coronary artery diseased vessels, left ventricular ejection fraction, percentage of residual stenosis and the smoking status.

In-hospital mortality. In the study group, 11 (3.7%) of the 295 patients died during hospitalization (7 from cardiogenic shock and 4 from left free wall rupture). The persistence of the occlusion of the infarct-related vessel was associated with a higher mortality (Table 2).

The patients in our study were taken from a larger, nonselected population of 368 consecutive patients. In this nonselected population, 36 patients died during their hospital stay. Four factors were correlated with in-hospital mortality; the patients who died were older (73.1 ± 9.6 years vs. 61.7 ± 13.4 years; p < 0.001), were predominantly women (47% vs. 21%; p < 0.001; OR 2.2), were more likely to have an anterior wall infarct location (67% vs. 46%; p = 0.02; OR 2.2) and were mainly nonsmokers (61% vs. 27%; p < 0.001; OR 3.6).

In the nonselected population, the multivariate analysis showed that three variables were independently associated with in-hospital mortality: absence of current smoking on admission, female gender and the anterior wall infarct location multiplied the risk of death by 2.4, 2.3 and 2.1, respectively. As mentioned previously, the multivariate analysis took confounding variables into account to determine the independent variables associated to in-hospital death.

Discussion

Thrombolysis and smoking in relation to the pathogenesis of the infarct-related artery occlusion in the setting of acute myocardial infarction. Our study suggests that in patients with acute myocardial infarction, thrombolysis is most effective in current smokers. One possible explanation may be that smoking increases the probability of thrombotic coronary artery occlusion (13–15). In acute myocardial infarction, the coronary occlusion consists of both arteriosclerotic tissue and thrombus, but their respective importance in a given occlusion is unknown. Smoking has been associated with platelet activation (16) and aggregation (17), coronary vasoconstriction, reduction of coronary flow reserve (18) and increased circulating levels of fibrinogen (19). The pathogenesis of coronary artery occlusion may thus be more thrombogenic than atherogenic in smokers, whereas in nonsmokers the occlusion may be predominantly due to the rupture or ulceration of the atheromatic plaque with the formation of clot rich in platelets, on which thrombolytic therapy has little effect. This hypothesis is further supported by our observation that in patients treated with thrombolytic agents, the rate of reopening of the infarct-related artery was similar in ex-smokers and nonsmokers, making the role of a different atherosclerotic process an unlikely explanation.

Recently, Mueller et al. (20) and Barbash et al. (21) reported significantly lower early reinfarction rates after myocardial infarction in smokers as compared with non- or ex-smokers. This may be consistent with our hypothesis, in which a lower rate of reinfarction is related to a decrease in thrombus formation owing to the widespread use of heparin and aspirin in the treatment of myocardial infarction. In smokers, Rivers et al. (22) have shown that the risk of reinfarction is significantly higher when tobacco consumption is continued, which supports the hypothesis that a thrombus plays an important role in the pathogenesis of myocardial infarction in smokers.

To our knowledge, the only report (23) on the influence of smoking on the reopening of the infarct-related artery reviewed the data base of the second Trial of Eminase in Acute Myocardial Infarction (TEAM-2) (24), in which all patients

received thrombolytic agents and artery patency was assessed within 90 to 240 min of the beginning of thrombolysis infusion. Smokers had a higher complete (TIMI flow grade 3) reopening rate of the infarct-related vessel, as compared with nonsmokers (66% vs. 51%; p = 0.007) (23). In our study, smokers exhibited a much higher reopening rate, defined by either TIMI flow grade 3 only or the combination of TIMI flow grades 2 and 3. Moreover, non- and ex-smokers did not benefit from thrombolysis in terms of coronary artery reopening.

Thrombolysis and myocardial infarct location. In our study, the anterior wall infarct location was an independent factor associated with coronary artery reopening. This finding was unexpected. Some investigators have reported higher reperfusion rates in the left anterior descending artery (25) and in inferior infarctions (23), and others found similar patency rates among the three arteries (26). Therefore, the reliability of our finding is suspect. One could hypothesize that a thrombogenic mechanism was predominant in different arteries from one study to another, but this discrepancy may very well be due to chance.

Implications. Smoking is a major risk factor for coronary artery disease and its discontinuance is associated with a reduction of the risk within 2 years (27–29) of quitting smoking. Smoking cessation must be encouraged to decrease the incidence of coronary artery disease as well as the incidence of numerous cancers. With the sharp decline in smoking prevalence among adolescents in the 1970s and 1980s (30), we should expect a decline in the incidence of myocardial infarctions in the future. If this is confirmed, the efficacy of thrombolysis may also be diminished because most myocardial infarctions will occur in nonsmokers. If further studies confirm our results, alternative therapeutic strategies to thrombolysis should be evaluated in nonsmokers.

Study limitations. Our study was an observational study, not a randomized trial, and some subjects did not receive thrombolytic therapy, which could influence the findings.

We assessed the coronary artery patency with variable delays. A standardized delay as well as repeat angiograms would have minimized the bias because of the physiologic variation of the infarct-related artery patency status with time (both for reopening and reocclusion) in the early phase of myocardial infarction. However, in our study, the time interval for coronary angiography corresponds to the plateau phase of the reopening rate of the infarct vessel (10), so that minimal variation should be expected.

Recent publications (31,32) challenge the conventional dogma that TIMI flow grades 2 and 3 are functionally equal with regard to effective infarct vessel reopening. We encompassed both TIMI flow grades 2 and 3 to define a patent vessel, but further analysis showed a similar relation between smoking, thrombolytic therapy and infarct-related artery patency, no matter how patency was defined.

In our study, no conclusions can be drawn from the mortality data with regard to the coronary artery patency status, because the study group was taken from a larger cohort of 368 consecutive patients, 73 of whom did not undergo coronary angiography.

Finally, our data on hemostatic/fibrinolytic system variables is incomplete; however, our initial aim was not to address this issue specifically. No relation was observed between fibrinogen level, hematocrit and platelets and the patency status of the infarct vessel or the smoking status. However, this lack of correlation may be the result of the small size of our patient group, because a correlation has been observed in other studies (33).

Conclusions. Our study suggests that in patients with acute myocardial infarction, thrombolysis is most effective in current smokers. If confirmed, our findings have practical implications for the management of acute myocardial infarction. Our results indicate that thrombolytic therapy should be proposed to smokers to reopen the infarct-related vessel, whereas other strategies, such as emergency coronary angioplasty, should be evaluated in further prospective studies in nonsmokers.

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