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Management of Acute Myocardial Infarction in Intensive Care Units in 1995: A Nationwide French Survey of Practice and Early Hospital Results

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Objectives. **This survey sought to determine actual practices in the management of acute myocardial infarction on a nationwide scale.**

Background. **Few data are available regarding the adoption of clinical trial results of treatment of myocardial infarction into "real-world" clinical practice.**

Methods. **Of 501 intensive care units in France, 373 (74%) collected data from all patients with myocardial infarction admitted within 48 h of symptom onset during November 1995.**

Results. **Data from 2,563 patients (71% men; mean age [±SD] 67 ± 14 years) were included. Time from symptom onset to admission was <6 h in 1,467 patients (62%). Thrombolysis was used in 822 patients (32%) and primary angioplasty in 330 (13%). The use of reperfusion therapy decreased markedly with age. During the first 5 days, heparin was prescribed in 96% of patients, aspirin in 89%, nitrates in 87%, beta-adrenergic blocking agents in 64%, angiotensin-converting enzyme inhibitors in 46% and calcium antagonists in 17%. Coronary angiography was performed in 33% of patients, and 58% had echocardiographic assessment of left ventricular ejection fraction (LVEF). Median LVEF was 50%. The 5-day mortality rate was 7.7% compared with 12.1% in a previous French survey carried out in 1984. By multivariate analysis, independent predictors of mortality were age, anterior infarction, history of stroke and heart failure and, when added to the model, Killip class and LVEF.**

Conclusions. **This survey shows that the results of therapeutic trials have largely translated to clinical practice, resulting in improved early outcome compared with the early 1980s. However, continuous efforts should be made to shorten the time delay before hospital admission and to increase the proportion of elderly patients receiving reperfusion therapy.**

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Acute myocardial infarction still represents a major cause of morbidity and mortality in industrialized countries (1–5). Over the past 15 years, there has been considerable progress in the understanding of its pathophysiologic mechanisms, as well as in its treatment at the acute stage. The major role of coronary thrombosis has been clearly established (6), and several prospective, randomized trials have conclusively shown the benefits of the early administration of antithrombotic medications (7,8). More recent evidence also suggests that primary angioplasty can at least equal the results of intravenous thrombolysis (9). In addition, the benefits of early administration of medications such as beta-adrenergic-blocking agents or angiotensin-converting enzyme (ACE) inhibitors is well documented (10–13), whereas it has been shown (14) that other classes of medications such as calcium antagonists should be avoided. Large-scale trials have also shown (15,16) substantially lower in-hospital mortality with the modern management of acute myocardial infarction. However, whether and to what extent these new data have actually influenced the everyday therapeutic management of patients presenting with acute myocardial infarction, on a nationwide scale remains speculative. The present prospective, observational study was therefore designed to assess the current practice of in-hospital management of acute myocardial infarction in intensive care units in France in 1995 and to analyze the results achieved in terms of early mortality.

Methods

Participating centers. The objective of the study was to obtain exhaustive data over a 1-month period from all institutions in the French health care system (i.e., university hospitals, public hospitals or private clinics) to which the patients are admitted. To this end, a list of all intensive care or coronary

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Abbreviations and Acronyms

ACE	=	angiotensin-converting enzyme
ECG	=	electrocardiogram, electrocardiographic
GUSTO-1	=	Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (trial)
LV	=	left ventricle, left ventricular
LVEF	=	left ventricular ejection fraction
MITI	=	Myocardial Infarction Triage and Intervention (trial)

care units admitting patients at the acute stage of myocardial infarction at the beginning of 1995 was established. All physicians in charge of these units were then asked to participate in the study. In all, 501 centers were listed: 47 university hospitals, 317 public hospitals and 137 private clinics, 373 of which finally participated in the study (74%). The participation rate was 94% (n = 44) for university hospitals, 76% (n = 242) for public hospitals and 64% (n = 87) for private clinics. One physician responsible for the study was recruited at each center and completed one form for each patient meeting the inclusion criteria and admitted to the intensive care unit during the study recruitment period. Patient care at each center was performed according to usual practice and independent of the study.

Patient selection. All consecutive patients admitted to the participating centers from November 1 to November 30, 1995 were included if they met the following criteria: 1) diagnosis of acute myocardial infarction based on the presence of serum enzyme elevation higher than twice the upper limit of normal for creatine kinase, aspartate transaminase or lactic dehydrogenase, alone or in combination, with a) chest pain lasting for at least 30 min and not relieved by nitrates, or b) electrocardiographic (ECG) changes on at least two contiguous leads with pathologic Q waves (at least 0.04 s) or persisting ST segment elevation or depression >0.1 mV, or both; and 2) time from the start of symptoms to admission to the intensive care unit <48 h.

Data collection. Cardiovascular history; risk factors (smoking status, history of hypertension or treated hypertension, cholesterol level >2.5 g/liter or treated hyperlipidemia, family history, diabetes mellitus); and clinical course over the first 5 days after admission, including maximal Killip class as well as the initial diagnostic and therapeutic management, were recorded for each patient. Furthermore, left ventricular ejection fraction (LVEF), when assessed at any time during the first 5 days, was recorded. The value for LVEF that was used for the present analyses was determined by the following priority ranking of the method used: 1) left ventricular (LV) contrast angiography; 2) radionuclide angiography; 3) echocardiography using the Simpson method; 4) echocardiography using the wall motion index of Berning and Steengaard-Hansen (17); 5) echocardiography with visual estimation of LVEF. For the present analyses, LVEF was categorized into four groups: 1) >50%; 2) 36% to 50%; 3) 21% to 35%; 4) ≤20%.

Table 1. Baseline Variables in All Patients Meeting Entry Criteria

Age (yr)	67 ± 14
Men	1,827 (71.3)
Women	736 (28.7)
Risk factors	
Smoking	782 (30.9)
Diabetes mellitus	440 (17.4)
Hyperlipidemia	910 (36.3)
Hypertension	1,157 (45.6)
Family history	404 (16.1)
Previous history	
PVD	269 (10.6)
Angina	1,032 (40.5)
Previous MI	460 (18.0)
CHF	228 (9.0)
Stroke	168 (6.6)

Data presented are mean value ± SD or number (%) of patients. CHF = congestive heart failure; MI = myocardial infarction; PVD = peripheral vascular disease.

Statistical analysis. Continuous variables are presented as mean value ± SD. Comparisons between groups were made using unpaired *t* tests for continuous variables and chi-square tests for discrete variables. Multivariate stepwise logistic regression analysis was used to assess the independent prognostic value of baseline variables. Variables with a p value <0.20 on univariate analyses were included in the models. Four models were used: 1) a model including only clinical and ECG variables at entry; 2) a model including clinical, ECG variables at entry and initial modality of treatment with primary coronary angioplasty or intravenous thrombolysis; 3) a model including baseline clinical and ECG variables, modality of initial treatment and worst Killip class during the first 5 days; and 4) a model including baseline clinical and ECG variables, modality of initial treatment, worst Killip class during the first 5 days and LVEF. Models 1 and 2 were used because Killip class and LVEF could have been determined late during the clinical course of the patients and were therefore not true admission data. Model 3 was used because LVEF was not measured in a substantial number of patients. A p value < 0.05 was considered significant for all tests.

Results

Baseline variables. A total of 2,800 case record forms were gathered, of which 317 had to be excluded for not meeting the entry criteria for the study; 49 corresponded to infarctions that occurred beyond the time limits of the study (i.e., late October or early December); in 211, the time from onset of symptoms to hospital admission exceeded 48 h; and 57 did not fulfill the required diagnostic criteria for acute myocardial infarction. Therefore, the study included 2,563 patients (mean age 67 ± 14 years; 1,827 men, 736 women) whose baseline characteristics are described in Table 1. The participation of centers and recruitment of patients according to a geographic subdivision into six administrative regions showed that the contribution of each region to the study was well balanced and varied from

Table 2. Relation Between Age Category and Use of Reperfusion-Oriented Strategy (intravenous thrombolysis or primary percutaneous transluminal coronary angioplasty)

	Age (yr)						p Value
	<50	51–60	61–70	71–75	76–80	>80	(chi-square test)
All pts (no.)	394	421	621	411	237	479	
Lysis or PTCA							
No.	253	263	334	166	67	69	< 0.0001
%	64	62.5	54	40	28	14	
Pts admitted <6 h after symptom onset (no.)	251	268	358	234	128	228	
Lysis or PTCA							
No.	208	207	254	138	50	52	< 0.0001
%	83	77	71	59	39	23	

PTCA = percutaneous transluminal coronary angioplasty; pts = patients.

12% to 19%, and the proportion of the total patient population for each region ranged from 14% to 20%.

The exact time to admission could not be determined in 186 patients (7.3%) but was presumed to be <48 h. When determined precisely, the median time from symptom onset to admission was 4 h 10 min and was <6 h in 1467 patients (62%).

On admission, chest pain was present in 2,148 patients (84%). The infarct territory was anterior in 775 patients (30%), inferior in 995 (39%) and lateral in 90 (3.5%), and 703 patients (27%) had a non-Q wave myocardial infarction or an infarct of undetermined location (left bundle branch block, pacemaker). The prevalence of a non-Q wave myocardial infarction was higher in patients >75 years old than in younger patients (31% vs. 26%, $p < 0.01$).

In-hospital management. Intravenous thrombolysis was administered in 822 patients (32%), of whom 123 had rescue coronary angioplasty within 24 h of hospital admission, and 330 (13%) had primary angioplasty. The use of either thrombolysis or primary coronary angioplasty was strongly related to length of time since symptom onset and age. In patients admitted within 6 h, 909 (62%) had either thrombolysis or coronary angioplasty compared with 147 (33%) for patients admitted from 6 to 12 h and 77 (17%) for patients admitted ≥12 h after symptom onset. In addition, a reperfusion-oriented strategy was used much less frequently in the older patients, with <30% of patients >75 years old and admitted within 6 h of symptom onset receiving intravenous thrombolysis or undergoing primary angioplasty (Table 2).

The medications used during the first 5 days after admission are represented in Figure 1. Heparin and aspirin were prescribed in 96% and 89% of patients, respectively. Beta-blockers were used in 64%, ACE inhibitors in 46% and calcium channel blocking agents in 17%. Use of beta-blockers and ACE inhibitors was related to LV failure and LVEF (Table 3). Use of beta-blockers decreased markedly with increasing severity of left heart failure and lower LVEF. Conversely, there was increasing usage of ACE inhibitors with increasing severity of heart failure or LV dysfunction, except for the most severe forms of LV dysfunction (Killip class IV and LVEF ≤20%).

Left heart catheterization was performed in 856 patients (33%), including those with primary angioplasty, and LVEF was calculated in 517 of them. Furthermore, 1,480 patients (58%) had at least one echocardiographic examination, and 26

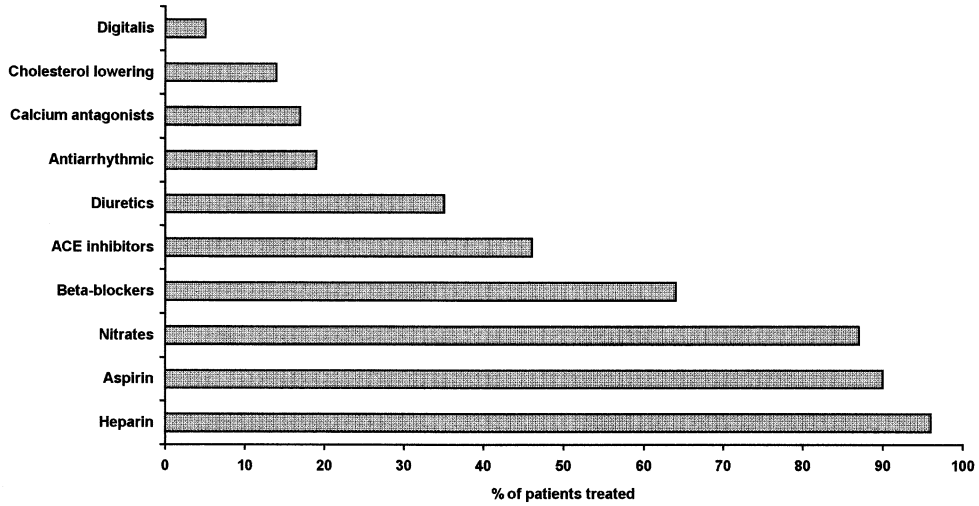

Figure 1. Medications used during first 5 days of hospital admission after infarction.

Table 3. Relation Between Usage of Beta-Adrenergic Blocking Agents or Angiotensin-Converting Enzyme Inhibitors and Killip Class or Left Ventricular Ejection Fraction

	Killip Class				
	I (n = 1,683)	II (n = 521)	III (n = 190)	IV (n = 169)	p Value (chi-square test)
Beta-blockers	1,320 (78%)	249 (48%)	45 (24%)	33 (20%)	< 0.0001
ACE inhibitors	698 (42%)	304 (58%)	117 (62%)	50 (30%)	< 0.0001
	LVEF				
	>50% (n = 823)	36–50% (n = 615)	21–35% (n = 238)	≤20% (n = 44)	
Beta-blockers	645 (78%)	429 (70%)	94 (39%)	11 (25%)	< 0.0001
ACE inhibitors	306 (37%)	350 (57%)	151 (63%)	19 (43%)	< 0.0001

Data presented are number (%) of patients. ACE = angiotensin-converting enzyme; LVEF = left ventricular ejection fraction.

(1%) underwent radionuclide LV angiography. On the whole, LVEF was determined within 5 days of hospital admission in 1,720 patients (67%). The median value of LVEF was 50%, with 16% of patients having severely depressed LV function (LVEF ≤35%).

During the first 5 days, cardiac surgery was performed in 17 patients (0.7%) and late coronary angioplasty in 29 (1.1%).

Clinical course and 5-day mortality. The complications observed during the first 5 days of the hospital period included ventricular arrhythmias in 796 patients (31%), recurrent angina in 533 (21%), conduction disturbances in 390 (15%), left heart failure in 359 (14%), supraventricular arrhythmias in 299 (12%) and mechanical complications in 106 (4%). The 1- and 5-day mortality rates were 2.2% (57 patients) and 7.7% (197 patients), respectively, and increased markedly with age (Fig. 2) and was double in women compared with men. Among clinical variables, diabetes mellitus, hypertension and history of angina, peripheral vascular disease, stroke or congestive heart failure were significantly related to a poorer in-hospital outcome, whereas smoking and known hyperlipidemia were related to an improved 5-day survival (Table 4). In addition, patients with a Q wave or anterior wall infarction or those in Killip class II or higher had a poorer prognosis. Patients receiving intravenous thrombolysis had a significantly improved outcome, and a trend for improved survival was also observed for patients undergoing primary angioplasty. Multivariate analyses showed that among admission variables, age, anterior wall myocardial infarction and history of stroke or congestive heart failure were independent predictors of survival; initial treatment modality (primary angioplasty or thrombolysis vs. no such treatment) was not an independent predictor of survival (Table 5).

Discussion

Representativeness of study sample. How the results of controlled studies of different treatment modalities in acute myocardial infarction translate into actually applied clinical practice on a large scale remains uncertain. To our knowledge, the present study is the first to analyze the current management of myocardial infarction in intensive care units (including a survey of both treatment modalities and diagnostic procedures used, with particular emphasis on determination of LV function) on a nationwide scale, irrespective of the type of

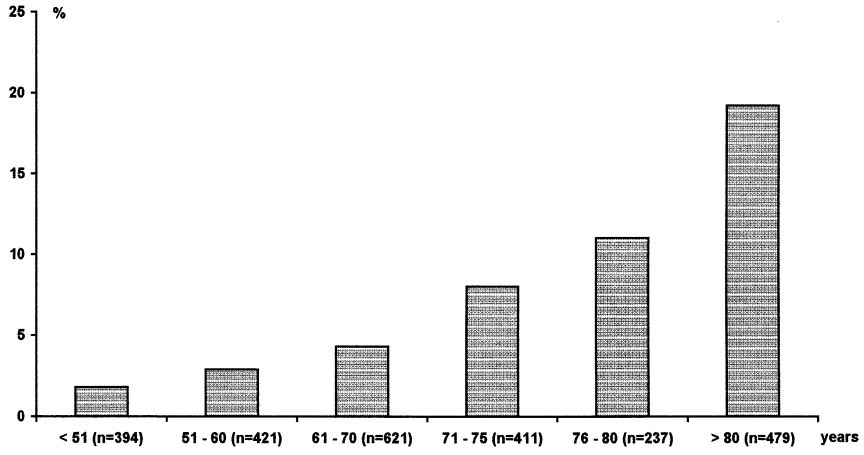

Figure 2. Five-day mortality according to patient age category.

Table 4. Univariate Analysis of Factors Related to Five-Day Mortality

	No. of Pts	Mortality at Day 5 [no. (%) of pts]	p Value
Age (yr)			
≤50	394	7 (1.8%)	
51–60	421	12 (2.9%)	
61–70	621	27 (4.3%)	
71–75	411	33 (8.0%)	
76–80	237	26 (11.0%)	
>80	479	92 (19.2%)	0.0001
Men	1,827	106 (5.8%)	
Women	736	91 (12.4%)	0.0001
Risk factors			
Family history			
No	2,102	161 (7.7%)	
Yes	404	21 (5.2%)	0.0808
Smoking			
No	1,746	165 (9.5%)	
Yes	782	26 (3.3%)	0.0001
Hypertension			
No	1,383	83 (6.0%)	
Yes	1,157	110 (9.5%)	0.0009
Diabetes mellitus			
No	2,087	147 (7.0%)	
Yes	440	45 (10.2%)	0.0220
Hyperlipidemia			
No	1,598	142 (8.9%)	
Yes	910	49 (5.4%)	0.0014
Previous history			
Angina			
No	1,515	101 (6.7%)	
Yes	1,032	92 (8.9%)	0.0353
MI			
No	2,103	152 (7.2%)	
Yes	460	45 (9.5%)	0.0624
CHF			
No	2,316	157 (6.8%)	
Yes	228	36 (15.8%)	0.0001
PVD			
No	2,279	161 (7.1%)	
Yes	269	31 (11.5%)	0.0088
Stroke			
No	2,383	168 (7.0%)	
Yes	168	26 (15.5%)	0.0001
Admission data			
Q wave MI			
No	692	39 (5.6%)	
Yes	1,820	151 (8.3%)	0.0242
Anterior wall MI			
No	1,788	106 (5.9%)	
Yes	775	91 (11.7%)	0.0001
Initial treatment modality			
Thrombolysis			
No	1,741	151 (8.7%)	0.0063
Yes	822	46 (5.6%)	
Primary PTCA			
No	2,233	178 (8.0%)	
Yes	330	19 (5.8%)	0.1588
Killip class			0.0001
I	1,683	37 (2.2%)	
II	521	39 (7.5%)	
III	190	28 (14.7%)	
IV	169	93 (55.0%)	

Abbreviations as in Tables 1 and 2.

Table 5. Multivariate Logistic Regression Analyses of Factors Related to Five-Day Mortality

	RR (95% CI)
Clinical and ECG Model	
Age (continuous)	1.07 (1.05–1.08)
Anterior wall MI	2.19 (1.58–3.06)
History of stroke	1.99 (1.22–3.23)
History of CHF	1.64 (1.06–2.56)
Clinical and ECG Model With Age as a Categoric Variable	
Age (vs. with age ≤50 yr)	
51–60 yr	1.54 (0.60–3.95)
61–70 yr	1.78 (0.96–3.31)
71–75 yr	3.01 (1.83–4.94)
76–80 yr	3.17 (1.92–5.22)
>80 yr	4.65 (3.33–6.47)
Anterior wall MI	2.12 (1.56–2.89)
History of stroke	1.81 (1.12–2.91)
Clinical, ECG and Treatment Modality Model	
Age (continuous)	1.07 (1.05–1.08)
Anterior wall MI	2.19 (1.58–3.06)
History of stroke	1.99 (1.22–3.23)
History of CHF	1.64 (1.06–2.56)
Clinical, ECG and Treatment Modality Model, Including Killip Class	
Age (continuous)	1.05 (1.03–1.07)
Anterior wall MI	1.97 (1.35–2.88)
History of stroke	2.03 (1.16–3.54)
Killip class	
II	2.05 (1.22–3.43)
III	3.61 (1.98–6.57)
IV	34.94 (9.65–126.48)
Clinical, ECG, Treatment Modality, Killip Class and LVEF Model	
Age (continuous)	1.06 (1.04–1.09)
Killip class	
II	1.41 (0.67–2.97)
III	2.36 (0.97–5.74)
IV	13.07 (6.26–27.28)
LVEF (%)	
36–50	3.20 (1.33–7.70)
21–35	7.01 (2.81–17.50)
≤20	14.30 (4.50–45.50)

CI = confidence interval; ECG = electrocardiographic; RR = relative risk; other abbreviations as in Tables 1 and 3.

admitting institution. The present survey may be considered highly representative of clinical practice in France by the end of 1995. Although the participation rate was higher in university hospitals, it remained satisfactory (>60%) for general hospitals and private clinics. In addition, when the recruitment of patients was analyzed according to a geographic subdivision into six administrative regions, no imbalance was seen from one region to another. The representativeness of the study sample is therefore likely to be adequate. From the results of the present study, it may be inferred that ~40,000 patients are admitted to an intensive care unit for recent acute myocardial infarction in France annually. However, this figure does not take into account the number of patients who die before

admission to an intensive care unit or those admitted >48 h after the onset of symptoms.

Time to admission. Our results show that the time delay before hospital admission is long and has remained virtually unchanged since the early 1980s: Only 62% of patients are admitted within 6 h of symptom onset, a rate similar to that observed in previous reports in France (18–20). This rate, which is particularly disappointing compared with that reported for other countries, deserves clarification as to the exact reasons for the delay in admission to hospital, and efforts at increasing public awareness are warranted. Recently, it has been shown (21) that a multimedia public campaign could result in a significant time savings to hospital admission in patients presenting with myocardial infarction, without an excess in hospital admissions for noncardiac chest pain.

Therapeutic management. In contrast, considerable changes have occurred in therapeutic management over the past decade (18,20,22,23). Reperfusion therapy, either by intravenous thrombolysis or primary angioplasty, is used in >60% of patients admitted within 3 h of symptom onset and in >50% of those admitted from 3 to 6 h. In all, 32% of all patients received intravenous thrombolysis, a figure that seems remarkably stable over time since the late 1980s (18–20) and from one country to another (1,24,25). However, these figures remain lower than expected because true contraindications to thrombolytic therapy are unusual (18). In particular, although the benefits of thrombolysis in elderly patients have been established (26,27), the proportion of elderly subjects presenting early after symptom onset who received intravenous thrombolysis remained abnormally low. This trend to an abnormally low usage of thrombolysis in elderly patients has also been reported in several other countries (28,29).

Conversely, the results of randomized trials of adjunctive medical treatment in acute myocardial infarction seem to have been largely translated into clinical practice. Compared with two, more limited, previous French multicenter surveys, carried out in 1988 (22) and 1991 (23), prescription of aspirin has increased from 63% to 79% and 89% in the present study, that of beta-blockers from 41% to 67% and 64%, that of ACE inhibitors from nil to 9% and 46% at present, whereas that of calcium antagonists has decreased from 62% to 35% and 17% in the present survey. Similar trends had also been noted in the French Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) centers (20) when medical prescriptions in 1985 and 1991 were compared. Compared with the figures reported from other countries in the early 1990s, the prescription of beta-blockers seems equivalent (25,30,31) or higher (29,32) and that of calcium antagonists lower (25,30,32). In a recently published survey of the prescription of beta-blockers by cardiologists in patients with a myocardial infarction in the United States in 1992, Brand et al. (33) report a 48% level of prescription in patients with no contraindications for beta-blocker use, stressing the insufficient level of compliance of cardiologists with their speciality's guidelines. In this regard, our results appear more encouraging and parallel those reported in Great Britain in a study (34) assessing the evolution of prescriptions from 1987 to 1989. The use of ACE inhibitors has almost doubled that observed in the early 1990s (25,30–32), which is evidence of the impact of recent trial results on ACE inhibitor use at the acute stage of infarction (10–13). In addition, the correlation that we found between prescription of ACE inhibitors and LV function shows that these medications were adequately prescribed. Prescription of aspirin has seldom been analyzed. In the Gruppo Italiano per lo Studio della Streptochiasi nell'Infarto Miocardico (GISSI) centers, Venturini et al. (28) found that only 64% of patients admitted for acute myocardial infarction received aspirin during the first hospital day. Whether prescription of these medications at the acute stage is followed by continued administration for secondary prevention at the chronic stage is uncertain, but it has been previously observed (35) that there was a comparative stability in drug prescription over the 5 years after an episode of myocardial infarction.

In-hospital outcome and early mortality. Our study was not designed to assess the therapeutic efficacy of any one medical or interventional treatment; however, it is striking to observe that the aforementioned changes in therapeutic management were accompanied by a marked reduction of early mortality compared with previous data collected in France. A previous multicenter French survey (18) carried out in 1984 showed a 5-day mortality rate of 12.1% in patients admitted to intensive care units and whose age was similar to patients in the present study. The present rate of 7.7% therefore represents a 36% decrease in early mortality over the past 11 years. Similar results were found in several other longitudinal studies in selected centers in France (36,37). A continued decline in early mortality in patients admitted with an acute myocardial infarction has also been reported in many other countries (1,25,29,34,38–40). The mortality rate in our study is comparable to that observed in the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-1) trial (16) and is also similar to that found in the community-wide Myocardial Infarction Triage and Intervention (MITI) survey in the United States (41). However, the results of the present pertain only to patients admitted to the hospital, not to those dying before hospital admission.

By univariate analysis, numerous factors were related to early mortality. However, after multivariate adjustment, only age, anterior wall infarction, history of congestive heart failure, previous history of stroke and Killip class were found to be independent correlates of mortality. LVEF, as measured in everyday practice, was also a major independent predictor of early mortality, although the statistical power of this factor was most likely reduced because it was frequently missing in patients who died very early. Age is a well known prognostic factor in patients admitted with an acute myocardial infarction. Killip class, LVEF and, to a lesser degree, anterior location of the infarct reflect the extent of myocardial damage and remain major indicators of early outcome. History of stroke is not usually analyzed in studies of prognostic indicators at the acute stage of infarction: Its independent prognostic significance stresses the prognostic importance of concomitant morbidity. Interestingly, age, Killip class and anterior infarction were also

three of the most potent predictors of mortality in patients with thrombolysis in the GUSTO-1 study (42), showing that similar predictive factors can be found in patients treated with intravenous thrombolysis and in unselected populations with myocardial infarction. Finally, reperfusion therapy by intravenous thrombolysis or primary angioplasty was related to early mortality by univariate but not by multivariate analysis. This finding, similar to that observed in the MITI study (41), can possibly be explained by the confounding influence of early left ventricular dysfunction. More important, the time point for assessing mortality in the present study may have been too early to evaluate the full impact of reperfusion therapy because it has been shown (43) that fibrinolytic therapy was associated with an increase in mortality in the first 2 days after administration that was counterbalanced by its favorable effects in the subsequent month.

Conclusions. The present nationwide study of patients admitted with an acute myocardial infarction in France confirms that the results of prospective trials, including recent data from ACE inhibitor trials, have been largely adopted into clinical practice (44). The resulting improvement in patient management has been accompanied by a marked decrease in early mortality. However, continuing efforts should be made to shorten the time delay before hospital admission, possibly by improving public awareness. In addition, to increase the proportion of elderly patients receiving reperfusion therapy, treating physicians should be made aware of the favourable benefit/risk ratio of thrombolysis in this specific category of patients.

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Appendix

*Participating Centers**

Alsace: Colmar (2), Haguenau, Mulhouse (3), Schiltigheim, Strasbourg (2), Wissenbourg. **Aquitaine**: Agen (2), Aire sur l'Adour, Arcachon, Bayonne (2), Bergerac, Biarritz, Bizanos, Bordeaux (2), Dax, Lesparre Médoc, Libourne, Marmande, Mérignac, Mont de Marsan, Orthez, Pau, Périgueux, Pessac, Sarlat. **Auvergne**: Aurillac, Clermont-Ferrand, Issoire, Mauriac, Montluçon (2), Moulins, Saint-Flour, Vichy. **Basse-Normandie**: Alençon, Argentan, Avranches, Bayeux, Caen, Cherbourg, Coutances, Flers, Granville, Lisieux, Saint-Lo, Trouville, Vire. **Bourgogne**: Autun, Auxerre, Beaune, Chalon sur Saône, Dijon, Le Creusot, Macon, Nevers, Paray le Monial, Semur en Auxois, Tonnerre, Fontaine les Dijon, Montceau les Mines. **Bretagne**: Brest (2), Dinan, Douarnenez, Fougères, Paimpol, Pont l'Abbé, Rennes (2), Saint Brieuc, Vannes. **Centre**: Blois, Bourges, Chambray les Tours, Chateauroux, Chinon, Dreux, Gasville Oiseme, Le Coudray, Nogent le Rotrou, Orléans (2), Saint Amand Montrond, Tours, Vendôme. **Champagne**: Chalons sur Marne, Chareleville Mezières, Chaumont, Epernay, Langres, Reims (2), Romilly sur Seine, Sedan, Saint Dizier, Troyes, Vitry le François. **Corse**: Ajaccio (2), Bastia. **Franche-Comté**: Belfort, Besançon (2), Lons le Saunier, Monbéliard, Pont d'Hery, Vesoul. **Haute-Normandie**: Bernay, Dieppe, Elbeuf, Evreux (2), Fecamp, Harfleur, Le Havre, Petit Quevilly, Pont-Audemer, Rouen (2), Vernon. **Ile de France**: Antony, Argenteuil, Aubervilliers, Aulnay sous Bois, Bagnolet, Bobigny, Boulogne-Billancourt, Briis sous Forge, Bry sur Marne, Champigny sur Marne, Clamart, Clichy, Corbeil Essonnes, Coulommiers, Créteil, Dourdan, Drancy, Evry, Fontainebleau, Garches, Gonesse, Issy les Moulineaux, Le Chesnay (2), Le Raincy, Mantes la Jolie, Meaux, Melun, Meulan, Montfermeil, Montmorency, Montreuil, Nanterre, Paris (13), Poissy, Pontoise, Port- Marly, Provins, Rambouillet, Rueil-Malmaison, Sèvres, Saint-Cloud, Saint-Denis (2), Saint-Mandé, Saint Maur des Fossés, Suresnes, Yerres. **Languedoc-Roussillon**: Alès, Bagnols sur Cèze, Béziers, Carcassonne, Montpellier (2), Narbonne (2), Nîmes (2), Perpignan (2), Sète. **Limousin**: Guéret, Limoges (3), Saint-Junien, Sainte Feyre, Saint Yrieix, Tulle, Ussel. **Lorraine**: Bar le Duc, Briey, Epinal (2), Essey les Nancy, Forbach, Freyming Merlebach, Metz, Nancy (2), Neufchateau, Remiremont, Saint Die (2), Thionville, Vandoeuvre lès Nancy, Verdun, Vittel. **Midi-Pyrénées**: Albi (2), Auch, Cahors, Castres (2), Cornebarrieu, Mazamet, Millau, Montauban (2), Muret, Saint Gaudens, Saint-Jean, Tarbes (2), Toulouse (4). **Nord**: Arras, Avesnes sur Helpe, Bethune, Bois Bernard, Boulogne sur Mer, Cambrai (2), Dechy, Dunkerque (2), Le Quesnoy, Lens, Lille (2), Lomme, Rang du Fliers, Roubaix, Tourcoing, Valenciennes, Wattrelos, Saint Pol sur Ternoise. **Pays de Loire**: Angers (2), Challans, Cholet, La Roche sur Yon, Laval, Le Mans (2), Les Sables d'Olonne, Nantes, Saumur, Saint Herblain, Saint Nazaire. **Picardie**: Abbeville, Amiens (3), Beauvais, Chauny, Creil (2), Hirson, Laon, Saint Quentin. **Poitou-Charentes**: Bressuire, Chatellererault (2), Cognac, Jonzac, La Rochelle, Niort (2), Poitiers, Rochefort, Royan, Saint Jean d'Angély, Saint Michel, Thouars. **Provence-Côte d'Azur**: Aix en Provence, Antibes, Arles, Aubagne (2), Avignon, Briançon, Cannes (2), Carpentras, Draguignan, Digne, Fréjus, Gap, Grasse, Hyères, Manosque, Marignane, Marseille (10), Martigues, Monace, Nice, Orange, Salon de Provence, Saint Laurent du Var, Toulon (2). **Rhône-Alpes**: Albertville, Annecy, Annonay, Belley, Bourg en Bresse, Bourgoin Jallieu, Chambéry, Feurs, Firminy, Givors, Grenoble (2), Lyon (4), Montbrison, Montélimar, Privas, Roanne, Romans sur Isère, Sallanches, Saint Chamond, Saint Etienne, Saint Jean de Maurienne, Saint Martin d'Heres, Saint Vallier, Thonon les Bains, Valence, Vienne, Villefranche, Voiron.

*Numbers in parentheses indicate the number of participating centers in each city, when more than one.

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