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Comparison of Thrombolysis Followed by Broad Use of Percutaneous Coronary Intervention With Primary Percutaneous Coronary Intervention for ST-Segment–Elevation Acute Myocardial Infarction Data From the French Registry on Acute ST-Elevation Myocardial Infarction (FAST-MI)

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Background—Intravenous thrombolysis remains a widely used treatment for ST-elevation myocardial infarction; however, it carries a higher risk of reinfarction than primary PCI (PPCI). There are few data comparing PPCI with thrombolysis followed by routine angiography and PCI. The purpose of the present study was to assess contemporary outcomes in ST-elevation myocardial infarction patients, with specific emphasis on comparing a pharmacoinvasive strategy (thrombolysis followed by routine angiography) with PPCI.

Methods and Results—This nationwide registry in France included 223 centers and 1714 patients over a 1-month period at the end of 2005, with 1-year follow-up. Sixty percent of the patients underwent reperfusion therapy, 33% with PPCI and 29% with intravenous thrombolysis (18% prehospital). At baseline, the Global Registry of Acute Coronary Events score was similar in thrombolysis and PPCI patients. Time to initiation of reperfusion therapy was significantly shorter in thrombolysis than in PPCI (median 130 versus 300 minutes). After thrombolysis, 96% of patients had coronary angiography, and 84% had subsequent PCI (58% within 24 hours). In-hospital mortality was 4.3% for thrombolysis and 5.0% for PPCI. In patients with thrombolysis, 30-day mortality was 9.2% when PCI was not used and 3.9% when PCI was subsequently performed (4.0% if PCI was performed in the same hospital and 3.3% if performed after transfer to another facility). One-year survival was 94% for thrombolysis and 92% for PPCI ($P=0.31$). After propensity score matching, 1-year survival was 94% and 93%, respectively.

Conclusions—When used early after the onset of symptoms, a pharmacoinvasive strategy that combines thrombolysis with a liberal use of PCI yields early and 1-year survival rates that are comparable to those of PPCI. (*Circulation*. 2008;118:268-276.)

Key Words: myocardial infarction ■ thrombolysis ■ angioplasty

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Randomized, controlled trials of thrombolytic therapy and primary coronary intervention (PPCI) in ST-elevation myocardial infarction have consistently shown the superiority of the interventional approach.^{1–3} However, in the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) trial, which was the only trial to compare percutaneous coronary intervention (PCI) and prehospital thrombolytic therapy (PHT), mortality was slightly but not significantly lower in the thrombolysis group,⁴ particularly in the subset of patients treated within 2 hours of symptom onset.⁵ In contrast, registry data are conflicting.^{6–10} In the early 1990s, several registries found no superiority of PCI over thrombolysis.^{6–8} More recently, a French registry performed at the end of 2000 showed that patients with PHT continued to have the best outcomes.⁹ In contrast, the large Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA) registry reported better results with primary PCI than with either in-hospital thrombolysis or PHT.¹⁰ In most of these studies, adjunctive pharmacological therapy, particularly antithrombotic medications, was not up to current standards, and the use of PCI after thrombolysis was low.¹⁰ Given these contradictory results, two key questions that remain are whether thrombolysis can still compete with PPCI now that its use has become widely disseminated and whether PCIs after thrombolysis are beneficial. The French registry of Acute ST-elevation and non-ST-elevation Myocardial Infarction (FAST-MI) is a nationwide registry promoted by the French Society of Cardiology and set up at the end of 2005. It included all patients admitted for myocardial infarction over a 1-month period at the participating institutions and specifically focused on the initial management of patients with ST-elevation myocardial infarction. This report describes the early and 12-month outcomes of ST-elevation myocardial infarction patients according to the use and modalities of reperfusion therapy at the acute stage.

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Methods

Population

The population and methods of the FAST-MI registry have been described in detail elsewhere.¹¹ Briefly, the objective of the study was to collect comprehensive data on the management and outcome of consecutive patients admitted to intensive care units for definite acute myocardial infarction over a 1-month period in France, irrespective of the type of institution to which the patients were admitted (ie, university hospitals, public hospitals, or private clinics, with or without on-site catheterization facilities). Of the 374 centers that treated patients with acute myocardial infarction at that time, 223 participated in the study (60%). One physician responsible for the study was recruited in each center and provided a complete list of all patients who met the inclusion criteria and who were admitted to the intensive care unit during the study recruitment period; the physicians in charge of the patients cared for them according to their usual practice, independent of the study.

Patient Selection

All consecutive adult (≥ 18 years of age) patients admitted to the participating centers for a 1-month period beginning on October 1, 2005, were included in the registry if they had (1) elevated serum

markers of myocardial necrosis more than twice the upper limit of normal for creatine kinase, creatine kinase-MB, or elevated troponins and (2) either symptoms compatible with acute myocardial infarction and/or ECG changes on at least 2 contiguous leads with pathological Q waves (at least 0.04 seconds) and/or persisting ST elevation or depression >0.1 mV. The time from the beginning of symptoms to admission to the intensive care unit had to be <48 hours. Patients with iatrogenic myocardial infarction were not included. For the present analysis, only patients with ST elevation or a presumed new left bundle-branch block on the initial ECG were included.

Patients gave informed consent for participation in the survey and late follow-up. The protocol was reviewed by the Committee for the Protection of Human Subjects in Biomedical Research of Saint Antoine University Hospital.

Data Collection

All data were recorded on computerized case record forms by dedicated research technicians who went to each of the centers at least once per week. An audit was performed in 3 of the 21 administrative regions and found complete concordance for $>90\%$ of the data collected. Cardiovascular history, current medication use at the time of admission, risk factors, and in-hospital clinical course (including maximal Killip class and initial diagnostic and therapeutic management) were recorded for each patient.

PHT was defined as the administration of thrombolytic therapy before hospital admission. Time to first call was defined as the time when the patient or his or her relatives first sought medical attention. For patients who used the mobile intensive care unit system (Service d'Aide Médicale Urgente [SAMU]) directly, time to first call was defined as the time to the initial call to the centralized regulation center and not as the time of ambulance arrival. Time to reperfusion was defined as time to (first) intravenous injection of thrombolytics or time to arterial puncture in patients treated with PPCI.

Rescue PCI was defined as PCI mandated by persisting symptoms or persisting ST-segment elevation 60 minutes or more after administration of thrombolysis. Systematic PCI after thrombolysis (pharmacoinvasive approach) was defined as PCI after coronary angiography that resulted from a systematic policy of combining thrombolysis with PCI in the absence of persisting or recurrent symptoms or persisting ST-segment elevation.

Recurrent myocardial infarction was defined as recurrent symptoms with a new rise in cardiac markers. Isolated troponin reelevation after PCI was not considered recurrent myocardial infarction in the absence of recurrent symptoms. Major bleeding was defined as any fatal or life-threatening bleeding or bleeding associated with a 15% decrease in hematocrit, a 5-g/dL fall in hemoglobin, or intracranial bleeding. Left ventricular ejection fraction was available in 81% of the patients, 60% determined by echocardiography and 35% by LV angiography. For the present analysis, we used the last value available before discharge.

Follow-up data were collected through contacts with the attending physicians, the patients, or their family. If missing, vital status was assessed from the registries of the patients' birthplaces. One-year follow-up was 99% complete.

Statistical Analysis

All continuous variables are described as mean \pm SD or median and interquartile range. All categorical variables are described with absolute and relative frequency distributions. Comparisons between groups used 1-way ANOVA and unpaired *t* tests or Mann-Whitney tests for continuous variables and χ^2 tests for discrete variables. Survival curves were generated by the Kaplan-Meier method and compared with log-rank tests. Cox multivariate regression analysis was used to assess predictors of 12-month outcome. Variables with $P < 0.10$ on univariate analyses were included in the multivariate models. We also performed a propensity analysis for the use of thrombolysis using a multivariate logistic regression model and developed a matched cohort of 1 PPCI patient for each thrombolysis patient, with matching on the propensity analysis score. For all tests, $P < 0.05$ was considered significant.

Table 1. Baseline Characteristics

	None (n=684), n (%)	Thrombolysis (n=466), n (%)	PPCI (n=564), n (%)	<i>P</i> , Overall	<i>P</i> , Lysis vs PPCI
Age, y	70.5±15.2	60.6±12.8	61.9±14.1	0.001	0.135
Female sex	266 (39)	98 (21)	148 (26)	0.001	0.051
Admission to general hospital	389 (57)	221 (47.5)	204 (36)	0.001	0.001
Admission to hospital with onsite PCI	453 (66)	370 (79)	530 (94)	0.001	0.001
Patients admitted to low-volume centers (≤10 cases per month)	165 (24)	69 (15)	61 (11)	0.001	0.055
Mean GRACE score	183±39	167.5±33	170±37	0.001	0.359
Admission heart rate, bpm (n=1708)	84±21	74±18	78±19	0.001	0.001
Admission systolic blood pressure, mm Hg (n=1706)	139±29	132±26	135±28	0.001	0.085
BMI, kg/m (n=1525)	27±5	27±4	27±5	0.41	0.525
Hypertension	422 (62)	190 (41)	263 (47)	0.001	0.059
Diabetes mellitus	175 (26)	64 (14)	105 (19)	0.001	0.035
Hypercholesterolemia	291 (43)	200 (43)	256 (45)	0.49	0.427
Current smoking	172 (25)	195 (42)	246 (44)	0.001	0.567
Family history	125 (18)	154 (33)	145 (26)	0.001	0.010
Previous MI	109 (16)	42 (9)	66 (12)	0.005	0.161
Previous PCI	71 (10)	33 (7)	57 (10)	0.24	0.087
Previous CABG	25 (4)	8 (2)	13 (2)	0.22	0.506
History of stroke	53 (8)	5 (1)	15 (3)	0.001	0.065
PAD	64 (9)	20 (4)	24 (4)	0.001	0.981
History of CHF	57 (8)	3 (1)	19 (3)	0.001	0.003
Chronic kidney disease	42 (6)	9 (2)	14 (2.5)	0.001	0.549
History of cancer	58 (8.5)	18 (4)	32 (6)	0.012	0.179
Asthma/COPD	30 (4)	7 (1.5)	16 (3)	0.047	0.149
Admission Killip class I	479 (70)	410 (88)	467 (83)	0.001	0.023
Anterior MI	259 (38)	163 (35)	225 (40)	0.45	0.105
Atrial fibrillation on admission	66 (10)	23 (5)	25 (4)	0.001	0.703
Typical chest pain	459 (67)	419 (90)	489 (87)	0.001	0.281
Cardiac arrest	6 (1)	18 (4)	16 (3)	0.018	0.625
Time from symptom onset to first contact <3 h	327 (48)	385 (83)	391 (69)	0.001	0.001
PCI during hospital stay	300 (44)	390 (84)	564 (100)	0.001	0.001
Medications before admission					
Antiplatelet agents	215 (31)	76 (16)	115 (20)	0.001	0.093
β-Blockers	158 (23)	75 (16)	97 (17)	0.005	0.636
Statins	161 (23.5)	100 (21.5)	119 (21)	0.60	0.888
ACE inhibitors	131 (19)	36 (8)	80 (14)	0.001	0.001
ARBs	117 (17)	41 (9)	62 (11)	0.001	0.243
CCBs (all)	121 (18)	52 (11)	84 (15)	0.021	0.078
CCBs (dihydropyridines)	90 (13)	37 (8)	48 (8.5)	0.012	0.740
Nitrates	79 (11.5)	20 (4)	36 (6)	0.001	0.141
Diuretics	190 (28)	52 (11)	98 (17)	0.001	0.005

BMI indicates body mass index; MI, myocardial infarction; CABG, coronary artery bypass grafting; PAD, peripheral arterial disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; and CCBs, calcium channel blockers.

Table 2. Time Delays According to Use and Type of Reperfusion Therapy

	PHT (n=301)	IHT (n=165)	Any Thrombolysis	PPCI	PPCI Without Transfer (n=510)	PPCI With Transfer (n=54)	No Reperfusion
Time to first call, min	60 (20–102)	73 (30–164)	60 (20–120)	75 (30–234)	75 (30–225)	96 (30–250)	180 (52–832)
Time to admission, min	180 (135–255)	120 (60–240)	170 (114–250)	180 (112–320)	180 (116–322)	180 (74–317)	330 (142–1073)
Time to reperfusion, min	110 (80–162)	195 (125–314)	130 (90–215)	300 (200–555)	290 (194–546)	425 (279–701)	...
Time from first call to reperfusion, min	45 (30–74)	90 (50–155)	57 (30–98)	170 (110–265)	165 (105–250)	245 (169–391)	...

IHT indicates in-hospital thrombolysis.
Values are median (interquartile range).

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Baseline Characteristics

Among the overall 1714 patients with persistent ST elevation or left bundle-branch block, 60% underwent reperfusion therapy. PPCI was the main reperfusion method (33%), whereas 29% received thrombolysis (two thirds, 18% of the entire population, were treated in the ambulance before hospital admission). The thrombolytic agent used was tenecteplase for 78% of the patients and other fibrin-specific agents in all remaining cases. The mobile intensive care units of the SAMU were used in 73% of the thrombolysis group and 59% of the PPCI group ($P<0.001$).

Patients without reperfusion therapy had an initial profile distinctly different from that of patients with either type of reperfusion treatment (Table 1). Overall, this subgroup was older and had a higher risk profile, as documented by a higher Global Registry of Acute Coronary Events (GRACE) risk score.¹² In contrast, patients treated with thrombolysis or PPCI had a similar GRACE score, although several of their initial characteristics differed.

Of the 466 patients treated with thrombolysis, 96% underwent coronary angiography during the hospital stay, 75% within 24 hours of the administration of lysis. PCI was performed during the hospital stay in 390 patients (84% of the thrombolysis group; median time from lysis to PCI 220 minutes). A pharmacoinvasive approach (systematic angiography with PCI) was used in 227 patients (58% of patients with PCI after lysis; median time from lysis to PCI 290 minutes), and a rescue or symptom-driven procedure was used in 144 patients (37%; median time to PCI 168 minutes). Of the latter patients, 80 (56%) underwent rescue PCI within 180 minutes of thrombolytic treatment.

Time Delays

As expected (Table 2), patients without reperfusion therapy presented later than the other groups. When we compared patients with thrombolysis and those with PPCI, time to first call was significantly longer in patients with PPCI (median 75 versus 60 minutes, $P<0.001$), but time from symptom onset to admission was similar (180 versus 170 minutes). Time to initiation of reperfusion therapy, however, was much longer

in patients with PPCI (time from symptom onset to reperfusion 300 versus 130 minutes; time from first call to reperfusion 170 versus 57 minutes). In patients whose first step had been to call the SAMU directly, time from first call to initiation of reperfusion therapy was longer by nearly 90 minutes when PPCI was used (130 minutes for PPCI versus 40 minutes for PHT and 85 minutes for in-hospital thrombolysis, $P<0.001$). This time delay, however, included the time for the SAMU to arrive on-site. Of note, there was a similar difference in time to initiation of reperfusion (45 minutes) between prehospital and in-hospital thrombolysis as between in-hospital thrombolysis and PPCI.

Concomitant Medical Therapy

Within the first 48 hours, glycoprotein IIb/IIIa inhibitors were administered much more often in PPCI patients. Low-molecular-weight heparin and clopidogrel were used slightly less often in thrombolysis patients; in patients not given chronic clopidogrel treatment, loading doses ≥ 300 mg were used in 72% of thrombolysis patients and 76% of PPCI patients. There was little difference in the use of statins, β -blockers, and angiotensin-converting enzyme inhibitors (Table 3).

At hospital discharge, compared with patients treated with PPCI, those treated with thrombolysis had a lower prescription of clopidogrel, angiotensin-converting enzyme inhibitors, and statins. The use of antiplatelet agents as a whole and β -blockers did not differ.

In-Hospital Outcomes

In-hospital mortality was the highest in patients without reperfusion therapy (9.5%); it was 5.0% in patients with PPCI and 4.3% in those with thrombolysis (prehospital 3.3%, in-hospital 6.1%). The causes of death were similar for patients with thrombolysis and PPCI (cardiac failure 55% versus 57%; sudden death or arrhythmias 30% versus 25%; other cardiovascular death 5% versus 7%; and noncardiovascular death 10% versus 11%). Overall, in-hospital complications were similar in patients treated with thrombolysis or PPCI (Table 3). There were 5 strokes in the thrombolysis group (1 fatal) and 4 in the PPCI group (none fatal). Left ventricular ejection fraction was significantly higher in patients with thrombolysis than in those with PPCI ($52.9\pm 11.9\%$ versus $50.4\pm 12.3\%$, $P=0.003$).

Table 3. Use of Concomitant Medications and In-Hospital Complications in Patients Treated With Thrombolysis or PPCI

	Thrombolysis, n (%)	PPCI, n (%)	<i>P</i>
Medications during the first 48 h	n=466	n=564	
Low-molecular-weight heparin	260 (56)	360 (64)	0.009
Glycoprotein IIb/IIIa inhibitors	76 (16)	386 (68)	<0.001
Clopidogrel	424 (91)	542 (96)	0.001
Statins	387 (83)	465 (82)	0.800
β-Blockers	363 (78)	425 (75)	0.338
ACE inhibitors	220 (47)	304 (54)	0.033
In-hospital complications			
Recurrent MI	9 (1.9)	5 (0.9)	0.149
Stroke	5 (1.1)	4 (0.7)	0.532
Maximal Killip class ≥II	82 (18)	114 (21)	0.237
Major bleeding	7 (1.7)	13 (2.3)	0.353
Transfusion	8 (1.7)	18 (3.2)	0.133
In-hospital death	20 (4.3)	28 (5.0)	0.610
Duration in ICU, d	4.6±5.6	4.4±4.2	0.779
Total duration in hospital, d	8.0±6.7	8.0±7.8	1.000
Medications at hospital discharge	n=446	n=536	
Any antiplatelet agent	405 (91)	502 (94)	0.094
Clopidogrel	371 (83)	478 (89)	0.009
Statins	367 (82)	470 (88)	0.018
β-Blockers	349 (78)	429 (80)	0.492
ACE inhibitors	273 (61)	363 (68)	0.033

ACE indicates angiotensin-converting enzyme; MI, myocardial infarction; and ICU, intensive care unit.

Thirty-Day Mortality According to Regional Policies, Timing of Reperfusion Therapy, and Use of Subsequent PCI in Patients With Thrombolysis

Among French regions, policies in the early management of patients with ST-elevation myocardial infarction differed; 5 regions (Alsace, Paris-Ile de France, Provence-Alpes-Côte d'Azur, Aquitaine, and Languedoc-Roussillon) had a preferential use of PPCI (>65%; average 69% PPCI), whereas all others used PPCI less often (average 47%). Thirty-day mortality was similar in the 5 regions with preferential use of PPCI (4.9%) and in the other regions (4.8%); in regions with >65% use of PPCI, 30-day mortality was 2.4% with thrombolysis and 5.4% with PPCI; in the other regions, the respective figures were 5.2% and 4.6%. None of these differences were statistically significant. Mortality was higher in low-volume centers (≤10 acute myocardial infarction patients per month) than in higher-volume centers (9.2% versus 4.2%, *P*=0.013).

In patients in whom reperfusion therapy was initiated within 6 hours of symptom onset, 30-day mortality was 4.4% with thrombolysis and 4.5% with PPCI (*P*=0.92). Beyond 6 hours, mortality was slightly higher with thrombolysis (7.7%) than with PPCI (5.7%; *P*=0.58; Table 4).

The thirty-day mortality rate was 9.2% in patients who did not undergo PCI and 3.9% in those who underwent PCI (*P*=0.044). The thirty-day mortality rate was 5.8% in those who underwent rescue or symptom-driven PCI versus 2.8% in those who had systematic PCI (*P*=0.147). PCI was performed after transfer to another institution in 91 patients (19.5%); 30-day mortality was 3.3% in PCI after transfer and 4.0% after PCI at the initial institution (*P*=0.752). Finally, when analyzed according to the timing of PCI after thrombolysis (according to quartiles of time delay from thrombolysis to PCI), 30-day mortality was 4.1% in the first and second quartiles (time from lysis to PCI ≤220 minutes) versus 3.6% in the third and fourth quartiles; mortality tended to be lower with increasing time from thrombolysis when PCI was performed on a systematic basis, whereas it tended to increase with increasing time from thrombolysis when PCI was performed as a rescue procedure (Figure 1). None of these differences, however, reached statistical significance, and the results can therefore only be considered indicative.

One-Year Survival

At 12 months, survival was 78.5% in patients without reperfusion therapy, 93.6% for thrombolysis (in-hospital 91.5%, prehospital 94.7%), and 91.8% for PPCI (*P*<0.001 for overall comparison; *P*=0.31 for comparison between thrombolysis and PPCI; Figure 2). In Cox univariate analysis, the OR for 1-year death in patients undergoing PPCI versus thrombolysis was 1.27 (95% CI 0.80 to 2.01). With Cox multivariate analysis, with or without inclusion of the propensity score, the type of reperfusion therapy was not found to be an independent correlate of survival at 12 months. Independent correlates comprised GRACE score, activity volume of the centers, comorbidities (stroke, chronic renal failure), and use of nitrates before the current episode.

To further adjust for the imbalances found at baseline between the groups with thrombolysis and PPCI, we assessed 12-month survival in 2 cohorts of patients matched on the propensity score of having thrombolysis rather than PPCI. One PPCI patient was matched for each thrombolysis patient (448 patients in each cohort). After matching, the 2 populations (thrombolysis versus PPCI) had a similar age (60.5±13 versus 60.9±14 years), similar risk factors, similar Killip class on admission, and similar risk scores (GRACE score 167.4±32.9 versus 167.7±35.6; GUSTO [Global Use of Strategies To Open coronary arteries] score 33±18 versus 35±20; and TIMI [Thrombolysis In Myocardial Infarction] score 22±11 versus 23±12). Among patients with

Table 4. Thirty-Day Mortality Rates in Patients With Intravenous Thrombolysis Versus PPCI According to Time From Symptom Onset to Reperfusion

	≤120 min (n=263)	121 to 180 min (n=183)	181 to 360 min (n=300)	>360 min (n=282)
Thrombolysis (n=465)	4.2% (9/216)	4.6% (5/108)	4.5% (4/89)	7.7% (4/52)
PPCI (n=563)	4.3% (2/47)	4.0% (3/75)	4.7% (10/211)	5.7% (13/230)

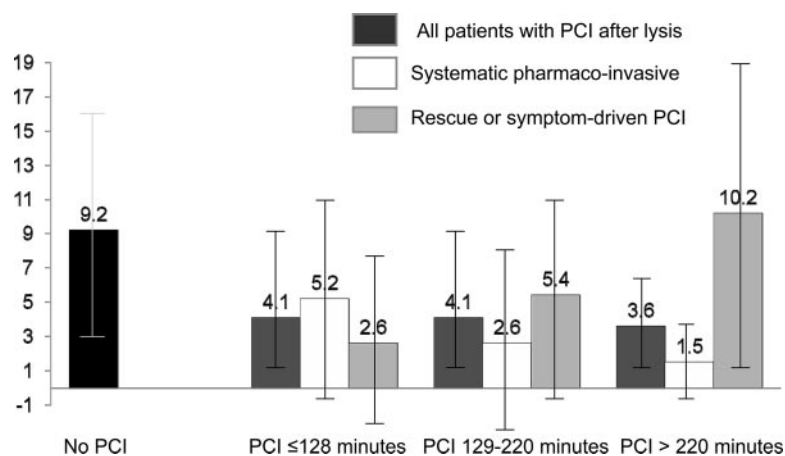


Figure 1. Thirty-day mortality in patients treated with thrombolysis, according to use and timing of subsequent PCI. Black bar indicates patients without PCI after thrombolysis; dark gray bars, all patients undergoing PCI after thrombolysis, whatever the reason for performing PCI; white bars, systematic PCI after thrombolysis (pharmacoinvasive approach); and light gray bars, rescue or symptom-driven PCI after thrombolysis. Vertical lines represent 95% CIs.

thrombolysis, 378 (84%) had a subsequent PCI during the hospital stay. Twelve-month survival was identical in the 2 groups (93.3% [95% CI 90.9% to 95.6%] for PPCI and 93.8% [95% CI 91.6 to 96.0%] for thrombolysis), and the hazard ratio for 1-year death (thrombolysis versus PPCI) was 0.94 (95% CI 0.56 to 1.57; $P=0.80$; Figure 3).

Discussion

The present survey reports contemporary data observed in patients with ST-elevation myocardial infarction in France, a country in which both the prehospital emergency care system and interventional cardiology are highly developed. Compared with previous French surveys,^{13,14} there was a marked increase in the use of both PPCI (from 13% in 1995 to 33% in 2005) and PHT (from 9.4% in 2000 to 17.6% in 2005). Concomitantly, early mortality strongly decreased over the past 10 years (5-day mortality 8.6% in 1995 and 4.0% in 2005). Importantly, intravenous thrombolysis was associated with outcomes similar to those of PPCI, given that nearly all patients (96%) underwent subsequent coronary angiography, and 84% underwent coronary interventions. Both multivariate

analyses and matched populations analyses showed that long-term (12-month) survival was comparable in patients treated with thrombolysis or PPCI. Of note, thrombolysis was initiated early after symptom onset, and most of the patients both in the thrombolysis and PPCI cohorts received recommended medications, both initially and at hospital discharge.

These results showing excellent outcomes with thrombolysis when used in properly selected subgroups of patients and with a de facto policy of routine subsequent invasive strategy are in keeping with both our previous findings⁹ and data from other important registries in which PHT was a currently used option. In the Vienna registry,¹⁵ PHT compared with PPCI was associated with encouraging mortality figures, as was PHT delivered by paramedics in the Canadian experience.¹⁶ These results are, however, in sharp contrast with those of the randomized, controlled trials comparing PPCI with intravenous thrombolysis (usually administered in-hospital), except those of the CAPTIM trial.¹⁻⁴ They also differ from those of the Swedish RIKS-HIA registry, which showed superior results with PPCI compared with either in-hospital thrombolysis or PHT.¹⁰ The same group, however,

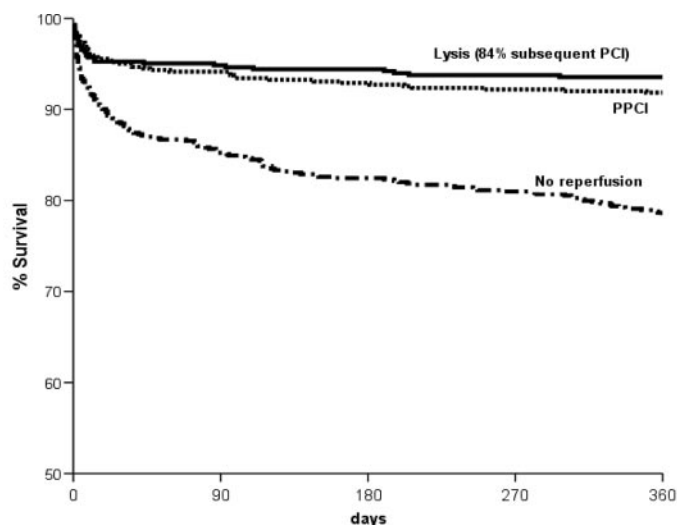


Figure 2. One-year survival according to use and type of reperfusion therapy.

# at risk	0	90	180	270	360
No reperfusion	581	562	552	534	534
Thrombolysis	440	437	434	433	433
PPCI	529	522	518	512	512

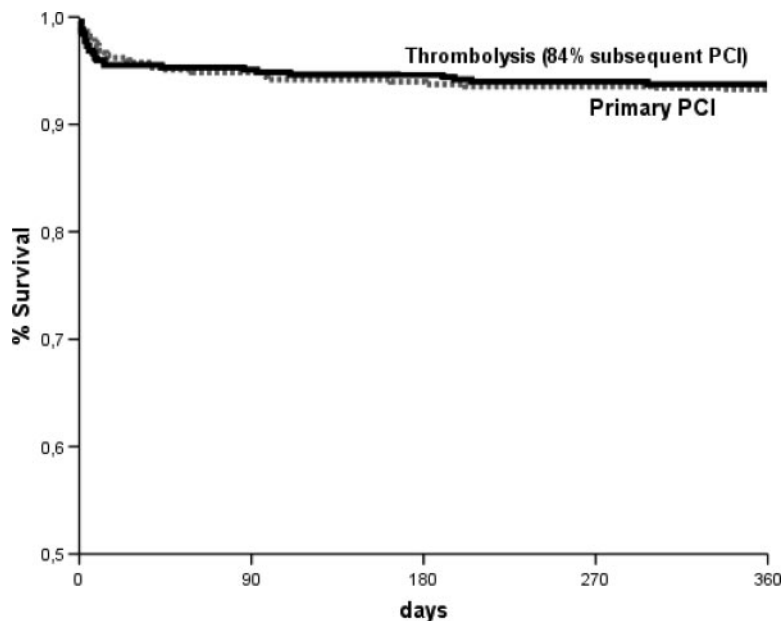


Figure 3. One-year survival in thrombolysis and PPCI patients matched on a propensity score of undergoing thrombolysis or PPCI. Of note, 96% of patients with thrombolysis underwent subsequent coronary angiography.

had reported much more encouraging results in the subset of patients who were transported by ambulance and received PHT. In that subset of patients, 1-year mortality was 7.2% compared with 7.6% in patients with PPCI during the same period of time in the same registry.¹⁷

Two points must be stressed with regard to the present study population with thrombolysis: (1) a vast majority (70%) had initiation of thrombolysis <3 hours after symptom onset, and (2) 96% underwent subsequent angiography, with 84% undergoing PCI (58% within 24 hours of receiving thrombolysis). The question of timing after symptom onset appears crucial in choosing the best mode of reperfusion therapy. In the CAPTIM randomized trial, patients randomized <2 hours after symptom onset had better survival when treated with PHT than with PPCI, whereas the reverse was true when thrombolysis was administered later.⁵ In the Vienna registry,¹⁵ mortality was lower with PHT than with PPCI when reperfusion therapy was initiated within 2 hours of symptom onset; afterward, PPCI was associated with lower mortality. In the present study population, time to initiation of reperfusion therapy was strikingly different according to the mode of reperfusion therapy chosen; in our real-world data, thrombolysis could be administered much earlier than PPCI. This longer time delay with PPCI likely explains why this technique did not yield better results than thrombolysis. In their enlightening analysis of the National Registry of Myocardial Infarction data, Pinto et al¹⁸ showed that the benefit of PPCI over thrombolysis was lost when the increased delay to delivery of reperfusion therapy compared with thrombolysis exceeded 114 minutes; in younger populations with anterior myocardial infarction, the equipoise could be much shorter, at 40 minutes.

Performance of PCI after thrombolysis also appears to be an important issue. In our previous registry, performed in 2000, we had shown that patients admitted to institutions with the capacity to perform PCIs had better outcomes than patients admitted to hospitals without catheterization labora-

tories, and this was true irrespective of the use of PPCI.¹⁹ As documented in the REACT (Rapid Early Action for Coronary Treatment) trial²⁰ and in a recent meta-analysis of 5 randomized trials,²¹ rescue PCI yielded results that were superior to those of repeat thrombolysis or abstention from any intervention in patients with no signs of reperfusion after intravenous thrombolysis. Likewise, in the meta-analysis of 3 randomized trials comparing systematic early PCI with delayed or ischemia-guided PCI in the stent era, systematic PCI was associated with a trend toward lower mortality and a significant reduction in the combined end point of death or reinfarction.²¹ More recently, the results of the Which Early ST-elevation myocardial infarction Therapy (WEST) trial showed that thrombolytic therapy followed by systematic PCI within 24 hours yielded results comparable to those of PPCI.²² Observational data have also shown that PCI after thrombolysis was associated with high procedural success rates and satisfactory clinical outcomes.^{23–25} Very recently, the results of the Combined Abciximab REteplase Stent Study (CARESS) trial confirmed that a policy of systematic PCI after thrombolysis was superior to a policy of PCI restricted to cases needing rescue based on symptoms and lack of resolution of ST elevation.²⁶ The question of the optimal timing of PCI after thrombolysis remains open. Among patients with thrombolysis in the present study, there was no difference in mortality according to the timing of PCI; however, in those with systematic PCI (as opposed to rescue or symptom-driven PCI), mortality was higher for patients who underwent PCI ≤ 128 minutes from the administration of thrombolysis (Figure 1).

This observation appears in keeping with the results of the ASSENT-4 trial (ASsessment of the Safety and Efficacy of a New Treatment strategy for acute myocardial infarction),²⁷ in which patients treated with thrombolysis followed by immediate PCI had an increased rate of reinfarction and a trend to higher mortality compared with patients receiving PPCI. This might be due to the presence of a prothrombotic

state immediately after thrombolysis. Interestingly, in the recently presented results of the FINESSE trial (Facilitated Intervention with Enhanced reperfusion Speed to Stop Events), in which thrombolysis was prescribed together with glycoprotein IIb/IIIa inhibitors, clinical outcomes were similar to those achieved with PPCI.²⁸ Whether a policy of PCI deferred for a few hours and a policy of a combination of early postthrombolysis PCI associated with glycoprotein IIb/IIIa inhibitors yield comparable results is still an unresolved issue.

The present study has the usual limitations of observational studies. National coverage was 60%, but the participating institutions reflected the broad spectrum of hospitals caring for acute myocardial infarction patients; in particular, they included both institutions with and those without on-site catheterization facilities, which accounted for the less than optimal timing of reperfusion therapy in a substantial proportion of the cases. Although time to reperfusion in patients treated with PPCI was long, it corresponded to the addition of time from symptom onset to first call and time from first call to reperfusion (165 minutes in nontransfer patients), the latter of which included the time for the SAMU ambulance to arrive on-site. Inclusion of patients at the participating institutions was consecutive, and the registry data were audited. This, however, does not preclude the possibility of confounding factors that might not have been recorded. Finally, as is the case for most observational studies, we did not have a formal hypothesis for ruling out differences between the 2 groups; given a 1-year mortality rate of 8.2% with PPCI, however, a 35% increased risk with thrombolysis (OR 1.35) would have been detected as statistically significant in the present study population by use of the Cox model. Overall, it is important that the present data be considered hypothesis generating and not as evidence of the formal equivalence of the 2 reperfusion methods.

Conclusions

In this nationwide survey of patients with ST-elevation myocardial infarction treated at the end of 2005 and receiving most of the recommended medications, thrombolysis yielded in-hospital and midterm results that were comparable to those of PPCI. These results, however, were achieved with a pharmacoinvasive strategy that combined thrombolysis with nearly universal coronary angiography and PCI in patients seen early after symptom onset. These findings might have important implications in terms of healthcare organization, because they suggest that semiurgent PCI preceded by timely thrombolysis may be an alternative to PPCI, without the need for widely disseminated catheterization laboratories to be available 24 hours per day, 7 days per week.

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Disclosures

Dr Danchin has received honoraria for participating in symposia organized by Boehringer Ingelheim, which manufactures thrombolytic agents. Dr Steg has been on the speakers' bureau for Boehringer-Ingelheim. Dr Blanchard has been on the speakers' bureau for Cordis and Boston Scientific. Dr Puel has acted as principal investigator for a registry sponsored by Boehringer-Ingelheim. Dr Goldstein is on the speakers' bureau for Boehringer-Ingelheim. The remaining authors report no conflicts.

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CLINICAL PERSPECTIVE

Primary percutaneous coronary intervention (PCI) is the best reperfusion method in patients with ST-elevation myocardial infarction, provided it can be performed in a timely manner. Because it remains difficult to implement on a large scale, however, intravenous thrombolysis is still used in many patients. This report presents data from a nationwide French registry collecting consecutive patients over a 1-month period at the end of 2005 and describes in-hospital and 1-year outcomes in patients treated with primary PCI or intravenous thrombolysis followed by routine coronary angiography in most patients (96%) and a very high rate of secondary PCI (84%). As expected, intravenous thrombolysis could be administered much more rapidly than primary PCI, particularly because two thirds of the patients received thrombolysis in the prehospital setting. There was no difference in early and late mortality between patients with primary PCI and those with a pharmacoinvasive strategy. One-year survival was similar among 2 cohorts of patients matched on a propensity score for receiving thrombolysis or primary PCI (93.8% and 93.3%). Overall, this study shows that the combination of intravenous thrombolysis with early PCI in patients seen in the first hours after symptom onset yields clinical results that compare with those of primary PCI. These findings may have important implications for healthcare organizations.

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