Impact of Prehospital Thrombolysis for Acute Myocardial Infarction on 1-Year Outcome

Results From the French Nationwide USIC 2000 Registry

Nicolas Danchin, MD; Didier Blanchard, MD; Philippe Gabriel Steg, MD; Patrick Sauval, MD; Guy Hanania, MD; Patrick Goldstein, MD; Jean-Pierre Cambou, MD; Pascal Guéret, MD; Laurent Vaur, MD; Youcef Boutalbi, MD; Nathalie Genès, MD; Jean-Marc Lablanche, MD; for the USIC 2000 Investigators

Background—Limited data are available on the impact of prehospital thrombolysis (PHT) in the "real-world" setting.

Methods and Results—Of 443 intensive care units in France, 369 (83%) prospectively collected all cases of infarction (≤48 hours of symptom onset) in November 2000; 1922 patients (median age, 67 years; 73% men) with ST-segment–elevation infarction were included, of whom 180 (9%) received intravenous thrombolysis before hospital admission (PHT). Patients with PHT were younger than those with in-hospital thrombolysis, primary percutaneous interventions, or no reperfusion therapy. Median time from symptom onset to hospital admission was 3.6 hours for PHT, 3.5 hours for in-hospital lysis, 3.2 hours for primary percutaneous interventions, and 12 hours for no reperfusion therapy. In-hospital death was 3.3% for PHT, 8.0% for in-hospital lysis, 6.7% for primary percutaneous interventions, and 12.2% for no reperfusion therapy. One-year survival was 94%, 89%, 89%, and 79%, respectively. In a multivariate analysis of predictors of 1-year survival, PHT was associated with a 0.49 relative risk of death (95% CI, 0.24 to 1.00; $P=0.05$). When the analysis was limited to patients receiving reperfusion therapy, the relative risk of death for PHT was 0.52 (95% CI, 0.25 to 1.08; $P=0.08$). In patients with PHT admitted in ≤3.5 hours, in-hospital mortality was 0% and 1-year survival was 99%.

Conclusions—The 1-year outcome of patients treated with PHT compares favorably with that of patients treated with other modes of reperfusion therapy; this favorable trend persists after multivariate adjustment. Patients with PHT admitted very early have a very high 1-year survival rate. **(*Circulation*. 2004;110:1909-1915.)**

Key Words: outcome assessment ■ intensive care ■ myocardial infarction ■ thrombolysis

Research in the 1990s has provided major information on the optimal management of patients with acute myocardial infarction (AMI) in terms of both acute reperfusion therapy and secondary prevention. In clinical trials, it has been shown that prehospital thrombolysis (PHT) could be used safely in patients presenting with evidence of AMI.[1] In a recent randomized trial comparing the outcome of patients treated with PHT with that of patients treated with primary percutaneous intervention (PCI), no statistically significant difference was observed in mortality or recurrent infarction and mortality rates between both techniques of reperfusion. Because the trial had to be stopped before inclusion of the total target population as a result of slow enrollment, no formal conclusions about the comparison of the 2 techniques can be drawn.[2] In the past 10 years, the French emergency medical system (Système d'Aide Médicale d'Urgence [SAMU]) has promoted the use of PHT through mobile intensive care units with a physician on board. Because data on the use of PHT in the real-world setting and on its prognostic impact are limited, we analyzed the data from a large prospective registry of patients admitted to hospital with AMI. This study was carried out in November 2000 throughout France.[3]

Methods

Population

The population and methods of the USIC 2000 registry have been described in detail elsewhere.[3] Briefly, the objective of the study was to gather complete and representative data on the management and outcome of patients admitted to intensive care units for definite AMI over a 1-month period in France, regardless of the type of institution to which the patients were admitted (ie, university hospitals, public hospitals, or private clinics). Of the 443 centers that treated patients with AMI at that time, 369 (83%) participated in the study. One physician responsible for the study was recruited in each center and completed a case record form for each patient meeting the inclusion

Received March 25, 2004; de novo received May 5, 2004; revision received June 9, 2004; accepted June 10, 2004.

From Service de Cardiologie, Hôpital Européen Georges Pompidou, Paris (N.D.); Clinique St Gatien, Tours (D.B.); Hôpital Bichat, Paris (P.G.S.); Hôpital Necker, Paris (P.S.); Centre Hospitalier d'Aulnay, Aulnay (G.H.); Centre Hospitalier Régional Universitaire de Lille, Lille (P. Goldstein, J.-M.L.); INSERM U 558, Toulouse (J.-P.C.); Hôpital Henri Mondor, Créteil (P. Guéret); and Laboratoire Aventis, Paris (L.V., Y.B., N.G.), France.

Correspondence to Nicolas Danchin, MD, FESC, FACC, Service de Cardiologie, Hôpital Européen Georges Pompidou, 20 Rue Leblanc, 75015 Paris, France. E-mail nicolas.danchin@egp.ap-hop-paris.fr

Circulation **is available at http://www.circulationaha.org** **DOI: 10.1161/01.CIR.0000143144.82338.36**

criteria and admitted to the intensive care unit during the study recruitment period. The physicians in charge of the patients took care of them according to their usual practice and independently from the study. The methodology of this prospective registry was similar to that of a previous survey carried out in France 5 years earlier,[4,5] although more data were collected in the more recent registry.

Patient Selection

All consecutive patients admitted to the participating centers from November 1 through 30, 2000, were included in the registry if they had (1) elevated serum markers of myocardial necrosis higher than twice the upper limit of normal for creatine kinase, creatine kinase-MB, or troponins and (2) symptoms compatible with AMI for ≥30 minutes and/or ECG changes on at least 2 contiguous leads with pathological Q waves (≥0.04 seconds) and/or persisting ST elevation or depression >0.1 mV. The time from symptom onset to admission to the intensive care unit had to be <48 hours.

For the present analysis, all patients had elevated enzymes or troponins measured during the hospital stay and had ST-segment elevation, a presumed new Q wave, or a presumed new left bundle-branch block on the first ECG recorded. Patients gave informed consent for participation in the survey and late follow-up.

Data Collection

Cardiovascular history, current medications at the time of admission, risk factors, in-hospital clinical course, including maximal Killip class, and initial diagnostic and therapeutic management were recorded for each patient. Furthermore, left ventricular ejection fraction, assessed at any time during the first 5 days, was recorded. PHT was defined as the beginning of thrombolytic treatment before hospital admission.

Statistical Analysis

All continuous variables, except time to admission, are given as mean±SD. All categorical variables are described using absolute and relative frequency distributions. Comparisons between groups were made with 1-way ANOVA, with unpaired *t* tests for continuous variables, and with χ^2 tests for discrete variables. Time to admission is expressed as median time with 25th and 75th percentiles; comparisons are made with the Mann-Whitney test. Multivariate stepwise logistic regression analysis was used to assess the independent prognostic value of baseline parameters on in-hospital outcome. Cox multivariate regression analysis was used for assessing predictors of 1-year outcome. Variables with a value of $P<0.10$ on univariate analyses were included in the models. Survival curves were generated with the Kaplan-Meier method and compared through the use of log-rank tests. For all tests, a value of $P<0.05$ was considered significant.

Results

Baseline Parameters

Of the 1922 patients initially included, 180 (9%) were treated with PHT, 365 (19%) had in-hospital thrombolysis, 434 (23%) had primary PCI, and 943 (49%) had no reperfusion therapy. Their baseline characteristics, risk factors, and previous cardiovascular histories are given in Table 1. Overall, patients receiving no reperfusion therapy were older and had a higher prevalence of risk factors and cardiovascular history. Among patients with reperfusion therapy, those receiving PHT were slightly younger (P=NS) and had fewer anterior infarctions. Slightly more patients with PHT had Killip class 1 on admission (88% versus 83%, P=NS). In addition, wide regional variations were observed in the type of reperfusion therapy used (Table 2). There were no marked differences in the medications used before the index episode (Table 3). Median time to admission was comparable in all patients who were treated with reperfusion therapy but was much longer in patients without reperfusion. Whereas virtually all patients with PHT (96%) were managed by the emergency system with mobile intensive care units, only 62% of those treated with either in-hospital thrombolysis or primary PCI were referred through this emergency channel ($P<0.001$).

Initial Management

Heparin (whether unfractionated or low molecular weight) and antiplatelet agents were used in a similar proportion of patients in each category (Table 3). In contrast, glycoprotein IIb/IIIa inhibitors were used much more frequently in patients who underwent primary PCI. β-Blockers and statins were used less often in patients without reperfusion therapy, but there was virtually no difference with regard to the use of ACE inhibitors. PCI was performed within 1 day of admission in a higher proportion of the patients with PHT (37%) compared with those with in-hospital thrombolysis (18%), primary PCI (0.7%), or no reperfusion therapy (12%).

In-Hospital Outcomes

Most in-hospital complications were observed in a similar proportion of patients in each category (Table 4). Deterioration of Killip class by at least 2 classes, however, was more frequent in patients with in-hospital thrombolysis or no reperfusion therapy. In-hospital mortality was particularly low (3.3%) in patients with PHT.

Medications at Hospital Discharge

There were no significant differences with regard to any of the 4 classes of secondary prevention medications between patients treated with the different modes of reperfusion therapy (Table 4). Antiplatelet agents, β-blockers, and statins, however, were prescribed less frequently in patients who did not receive reperfusion therapy.

One-Year Survival

One-year survival was 94% in patients with PHT, 89% in patients with either in-hospital thrombolysis or primary PCI, and 79% in patients without reperfusion therapy ($P<0.0001$; Figure 1). Multivariate analysis showed that older age, history of peripheral vascular disease, anterior location of infarction, presence of diabetes mellitus, history of congestive heart failure, and history of renal failure were independent predictors of higher 1-year mortality. Conversely, PHT was associated with lower 1-year mortality (relative risk, 0.49; 95% CI, 0.24 to 1.00; $P=0.05$; Table 5).

PHT According to Time to Admission

The median time from symptom onset to admission in patients with PHT was 3.5 hours. Comparison of patients admitted before or after 3.5 hours (Table 6) shows that there were no differences in demographic characteristics, location of infarction, or management during the current hospital admission. In-hospital complications were less frequent in patients with early PHT. Both in-hospital mortality and 1-year mortality were dependent on the time from symptom onset to hospital admission. When time to admission was below the median, in-hospital mortality was nil and 1-year

TABLE 1. Baseline Characteristics According to Type of Reperfusion Therapy

Variable	Prehospital Lysis (n=180)	In-Hospital Lysis (n=365)	Primary PCI (n=434)	No Reperfusion Therapy (n=943)
Age, mean±SD, y	59±13*	61±14	61±14	69±14
Age, median (25th–75th percentiles), y	59 (49–70)	64 (50–73)	62 (50–72)	71 (59–80)
Female sex, n (%)	29 (16)*†	90 (25)	98 (23)	304 (32)
Risk factors, n (%)				
Diabetes mellitus	22 (12)*†	54 (15)	89 (20.5)	231 (24.5)
Past smoking	45 (25)	83 (23)	109 (25)	223 (24)
Current smoking	91 (51)*†	134 (37)	183 (42)	252 (27)
Hyperlipidemia	67 (38.5)	156 (43)	175 (41)	359 (39)
Hypertension	58 (32)*	143 (39)	169 (39)	487 (52)
Previous history, n (%)				
Previous MI	18 (10)*	37 (10)	75 (17)	170 (18)
CHF	4 (2)*	5 (1)	10 (2)	92 (10)
Stroke	2 (1)	10 (3)	16 (4)	56 (6)
CABG	3 (2)	8 (2)	12 (3)	34 (4)
PCI	12 (7)	22 (6)	55 (13)	64 (7)
Peripheral vascular disease	8 (4.5)*	18 (5)	23 (5)	117 (12)
Renal insufficiency	2 (1)*	4 (1)	13 (3)	65 (7)
Current episode of MI				
Median time to admission (25th–75th percentiles), h	3.5 (2.5–5.7)	3.5 (2.2–6.0)	3.25 (2.2–5.2)	11.7 (4.5–24.0)
Anterior MI, n (%)	61 (34)†	139 (38)	201 (46)	349 (37)
Killip class on admission, n (%)				
I	159 (88)*	313 (86)	353 (81.5)	665 (71)
II	17 (9)	36 (10)	50 (11.5)	164 (17)
III	2 (1)	6 (2)	13 (3)	85 (9)
IV	2 (1)	8 (2)	17 (4)	28 (3)
Admission heart rate, bpm	75±18*	76±17	78±18	81±20
Initial systolic blood pressure, mm Hg	127±23*	133±27	130±26	135±28

CHF indicates congestive heart failure.
*$P<0.05$ vs no reperfusion therapy; †$P<0.05$ vs other modes of reperfusion therapy.

survival was 99% (Figure 2); when time to admission was over the median value, in-hospital mortality was 6.0% and 1-year survival was 90% ($P=0.01$). Cox multivariate analysis showed that time to admission above median (>3.5 hours) was associated with an increased risk of mortality (OR, 9.05; 95% CI, 1.09 to 75.0; $P=0.04$), together with older age (OR, 1.07; 95% CI, 1.00 to 1.13; $P=0.04$) and use of antiplatelet agents before admission (OR, 4.57; 95% CI, 1.08 to 19.2; $P=0.04$).

Discussion

The present study analyzes the current management of patients with AMI admitted to intensive care units on the scale of a whole country, regardless of the type of institution to which the patients were admitted. Participation was high in all types of institutions (academic, general hospitals, private clinics); no imbalance was seen from one region to another; and the data are highly concordant with those of a previous French registry based on a similar methodology 5 years earlier.[4] It may therefore be considered highly representative of the practice in France by the end of 2000.

The French system of management of prehospital medical emergencies is based on a permanent, centralized call system that dispatches fully equipped ambulances with a physician on board to the sites of supposed medical emergencies. According to the situation for each case, including distance from a catheterization laboratory, traffic, and immediate availability of a catheterization team,

TABLE 2. Regional Variations in Use of Reperfusion Therapy

	Ile de France	Northwest	Northeast	Center	Southwest	Southeast
PHT, n (%)	41 (26)	39 (22)	14 (7)	31 (24)	19 (11)	36 (24)
In-hospital lysis, n (%)	16 (10)	85 (47)	93 (48)	53 (42)	69 (42)	49 (32)
Primary PCI, n (%)	102 (64)	56 (31)	88 (45)	43 (34)	78 (47)	67 (44)

TABLE 3. Medical Management Before Hospital Admission and During the First 48 Hours

Variable	Prehospital Lysis, n (%) (n=180)	In-Hospital Lysis, n (%) (n=365)	Primary PCI, n (%) (n=434)	No Reperfusion, n (%) (n=943)
Medications used before current episode				
Antiplatelet agents	34 (19)	67 (18)	91 (21)	240 (25)
β-Blockers	28 (16)	65 (18)	82 (19)	179 (19)
ACE inhibitors	18 (10)†	35 (10)	51 (12)	176 (19)
Statins	28 (16)	62 (17)	80 (18)	153 (16)
Medications used during first 48 h after admission				
Unfractionated heparin	166 (92)†§	318 (87)	350 (81)	675 (72)
Low-molecular-weight heparin	39 (22)†§	61 (17)	142 (33)	297 (32)
GP IIb/IIIa inhibitors	22 (12)§	31 (9)	201 (46)	102 (11)
Antiplatelet agents	175 (97)*	348 (95)	430 (99)	873 (93)
β-Blockers	153 (85)†‡	283 (78)	341 (79)	596 (63)
ACE inhibitors	76 (42)	145 (40)	184 (42)	378 (40)
Statins	103 (57)†	178 (49)	222 (51)	365 (39)
PCI within 1 d of admission	67 (37)	66 (18)	3 (0.7)	117 (12)

GP indicates glycoprotein.
*$P<0.05$, †$P<0.01$ vs no reperfusion therapy.
‡$P<0.05$ vs in-hospital thrombolysis.
§$P<0.01$ vs primary PCI.

the physician on board may opt for PHT, primary PCI, or conservative management. In addition, there were important regional variations in the use of the different modes of reperfusion therapy (Table 2). Among patients receiving reperfusion therapy, the proportion of PHT use varied from 7% to 26% and that of primary PCI from 31% to 64% across the 6 main French administrative regions. When included in the multivariate analyses, however, regions were not independent predictors of outcome. Our data show that the 1-year outcome of patients treated with PHT compares favorably with that of patients treated with other modes of reperfusion therapy and that the use of PHT was an independent predictor of improved 1-year survival. In addition, patients treated very early (ie, those admitted within 3.5 hours of the onset of chest pain) had extremely low 1-year mortality figures.

TABLE 4. In-Hospital Events and Discharge Medications (Percentage of Patients)

Variable	Prehospital Lysis, %	In-Hospital Lysis, %	Primary PCI, %	No Reperfusion, %
Maximum Killip class during first 5 d				
I	142 (79)†	270 (75)	325 (75)	580 (62)
II/III	33 (18)	72 (20)	75 (17)	276 (29)
IV	5 (3)	20 (5.5)	34 (8)	83 (9)
Killip class deterioration ≥2 classes	4 (2)*	22 (6)	14 (3)	58 (6)
Reinfarction	5 (3)	6 (2)	5 (1)	22 (2)
Ventricular fibrillation	7 (4)	17 (5)	22 (5)	24 (3)
Atrial fibrillation	10 (6)	22 (6)	31 (7)	95 (10)
Second- or third-degree AV block	9 (5)	13 (4)	25 (6)	54 (6)
Left ventricular ejection fraction ≤35%	13 (8)†	28 (8.5)	51 (13)	145 (18)
Stroke	2 (1.1)	5 (1.4)	1 (0.2)	11 (1.2)
In-hospital mortality	6 (3.3)‡	29 (8.0)	29 (6.7)	115 (12.2)
Discharge medications				
Antiplatelet agents	167 (96)	325 (97)	395 (97.5)	766 (92.5)
β-Blockers	146 (84)†	276 (82)	338 (83.5)	569 (69)
ACE inhibitors	100 (57.5)	173 (51.5)	220 (54)	419 (51)
Statins	133 (76)†	230 (68.5)	289 (71)	471 (57)

*$P<0.05$, †$P<0.01$ vs no reperfusion therapy.
‡$P<0.05$ vs hospital thrombolysis.

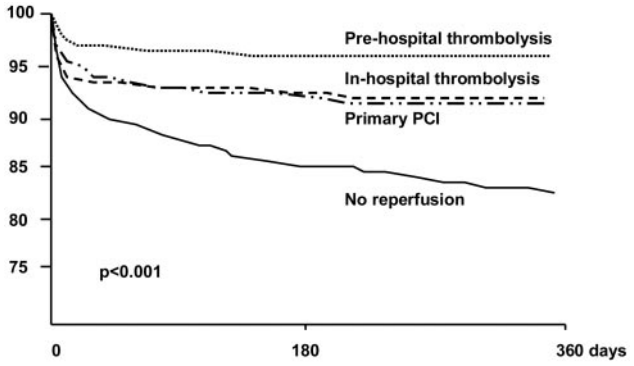

Figure 1. Age-adjusted Kaplan-Meier 1-year survival according to reperfusion strategy. After adjustment by Cox multivariable analysis, PHT remained associated with improved survival.

Although randomized trials comparing primary angioplasty and intravenous thrombolysis have consistently shown the superiority of the former mode of reperfusion therapy,[6] they have obvious methodological limitations and cannot be considered a reflection of what is observed in everyday life. Additionally, most registries assessing the impact of the 2 reperfusion techniques in the real world have documented equivalent results,[5,7,8] suggesting that the organizational difficulties in implementing emergency angioplasty on a large scale might attenuate the beneficial effects demonstrated in highly specialized centers during the time period when they participated in the randomized trials. Therefore, it is not altogether surprising that PHT may achieve even better results than conventional thrombolysis.

The efficacy of PHT has initially been demonstrated in the Grampian Region Early Anistreplase Trial (GREAT),[9] in which administration of thrombolysis by the general practitioners before hospital admission resulted in a 50% reduction in 1-year mortality. In this trial, which was set up in a rural area, most of the difference was observed in the 180 patients who had ST-segment elevation or left bundle-branch block on their first ECG. Recently, a meta-analysis of 6 trials comparing PHT and in-hospital thrombolysis confirmed this beneficial effect, showing a 17% reduction in in-hospital mortality with the use of PHT.[1] In the Comparison of Angioplasty and Prehospital Thrombolysis In acute Myocardial infarction (CAPTIM) trial,[2] which compared PHT with primary PCI, 1-month mortality was lower (although not significantly so) in the group that received PHT.

Two factors may explain the results observed in our population. The first factor is the time gained compared with in-hospital thrombolysis. The time delay from symptom onset to hospital admission was similar in the PHT, in-hospital thrombolysis, and primary PCI groups; however, patients in the PHT group had already received reperfusion treatment when they arrived at the intensive care unit. In this regard, in the GREAT trial,[9] there was a 2.25-hour time gain in the 163 patients in whom thrombolysis was administered before hospital admission. Likewise, in the CAPTIM trial,[2] time to onset of reperfusion therapy was shorter by 60 minutes in the PHT group. Of note, in the patients with PHT who reached the hospital after 3.5 hours (median time to admission in this group), the outcome was comparable to that of the patients with in-hospital thrombolysis. In the CAPTIM population, PHT appeared superior to primary angioplasty in the patients in whom thrombolytic treatment could be administered before 2 hours from symptom onset.[10] These data are concordant with the observation from the meta-analysis of trials of thrombolytic therapy that showed an exponential decrease in the efficacy of thrombolysis in the patients treated >3 hours of the onset of chest pain.[11] In this regard, it is now clear that myocardial salvage is highly dependent on the time from the beginning of symptoms to reperfusion[12] and that very early administration of thrombolytics is likely to result in superior myocardial salvage compared with in-hospital thrombolysis and possibly also primary PCI, for which the time delay observed in the real-world setting is often ≥1 hour.[13] Of note, the proportion of patients with Killip class 4 on arrival to the hospital was lower with PHT than observed in all other subgroups. This finding is concordant with the observations from the CAPTIM trial,[10] but it may also reflect a selection bias, with patients in cardiogenic shock before hospital admission being oriented preferentially toward the catheterization laboratory for primary PCI.

Second, a high proportion of our patients treated with PHT in our registry underwent rapid coronary angiography and angioplasty (37% within 1 day of admission, 67% during the initial hospital stay). The percentage of patients receiving of early angioplasty is similar to that observed in France in the CAPTIM trial (33%)[2] and considerably higher than that observed in other trials comparing thrombolysis and primary PCI such as the DANish multicenter randomized study of fibrinolytic therapy versus acute coronary angioplasty in Acute Myocardial Infarction (DANAMI-2) trial.[14] In-hospital use of coronary angioplasty is also higher than that (40%) reported in the Euro Heart Survey of Acute Coronary Syndromes.[15] Such a liberal use of early PCI after thrombolysis is likely to result in a decreased rate of reinfarction (reinfarction rate in our PHT group was only 3%) and improved long-term outcome. Previous data have shown that combined PHT and systematic urgent PCI with stenting in patients with AMI yielded excellent results, with only 2.3% reinfarction rates and 90% 2-year infarct-free survival.[16] Likewise, the results obtained with PHT associated with provisional rescue angioplasty in patients with a completely occluded infarct-related artery on the 90-minute angiogram are excellent.[17] Furthermore, the long-term results of GREAT show that most of the benefit of PHT is observed during the first 2 years after the acute event and that the survival curves of patients with PHT or hospital thrombolysis converge beyond this time

TABLE 5. Multivariate Predictors of 1-Year Mortality

	OR	95 % CI	*P*
Age	1.06	1.05–1.07	0.0001
Peripheral vascular disease	1.78	1.29–2.45	0.0001
AMI	1.65	1.30–2.10	0.0001
Diabetes mellitus	1.62	1.25–2.09	0.0001
Prior congestive heart failure	1.61	1.13–2.27	0.0008
Renal failure	1.56	1.06–2.29	0.03
PHT	0.49	0.24–1.00	0.05

TABLE 6. Characteristics and Outcome of Patients With PHT According to the Time From Symptom Onset to Hospital Admission

Variable	Time to Admission ≤3.5 h (n=85)	Time to Admission >3.5 h (n=87)	P
Age, mean±SD, y	59±13	61±13	NS
Female sex, n (%)	12 (14)	13 (15)	NS
Time to admission, median (25th–75th percentiles), h	2.5 (2.2–3.0)	5.75 (4.75–8.50)	0.0001
Anterior MI, n (%)	25 (29)	33 (38)	NS
Admission to center with onsite angioplasty facilities, n (%)	57 (67)	66 (76)	NS
In-hospital management, n (%)			
Oral antiplatelet agents	82 (96.5)	86 (98)	NS
GP IIb/IIIa inhibitors	11 (13)	11 (13)	NS
β-Blockers	74 (87)	71 (82)	NS
ACE inhibitors	38 (45)	36 (41)	NS
Statins	49 (58)	49 (56)	NS
Early PCI (day 0 or 1)	31 (36.5)	33 (38)	NS
PCI during hospital stay	57 (68)	57 (66)	NS
In-hospital complications, n (%)			
Killip class on admission >1	4 (5)	14 (15)	0.07
Maximum Killip class during first 5 d >1	13 (15)	21 (24)	0.06
Left ventricular ejection fraction >50%	51 (60)	44 (51)	0.08
Ventricular fibrillation	4 (5)	3 (3.5)	NS
Atrial fibrillation	2 (2)	7 (8)	0.09
Stroke	1 (1)	1 (1)	NS
5-d Mortality, n (%)	0	4 (5)	0.04
30-d Mortality, n (%)	0	6 (7)	0.01

GP indicates glycoprotein.

point.[18] Early revascularization of the culprit artery might therefore help to avoid the subsequent deterioration of the initial beneficial result of very early thrombolysis. Consistent with the CAPTIM[2] and PRimary Angioplasty in patients transferred from General community hospitals to specialized PTCA Units with or without Emergency thrombolysis (PRAGUE)-2[19] data, we found that "late" PHT resulted in a similar outcome compared with primary angioplasty and in-hospital thrombolysis. These results combined suggest that the benefits of thrombolytic therapy and primary PCI may be different according to the time elapsed since the onset of symptoms, which may have evident clinical implications when the most appropriate mode of reperfusion therapy at the acute stage of myocardial infarction is chosen.

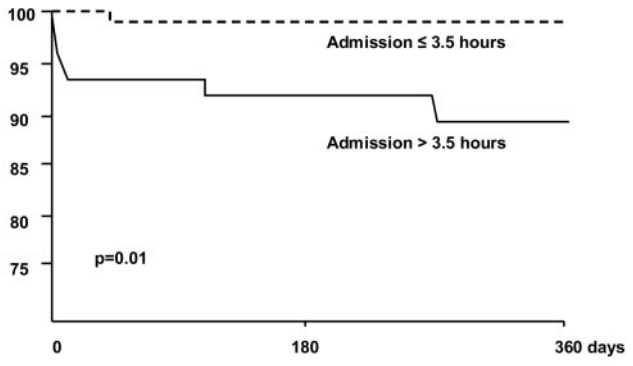

Figure 2. One-year survival in patients with PHT according to time to admission.

This prospective survey does not have the methodological strength of randomized trials. However, one merit is that it reflects the results achieved in the real world outside the constraining limits of a randomized trial. Using a threshold of 1-mm ST elevation in the anterior and inferior leads for inclusion might be considered not stringent enough; however, myocardial infarction was confirmed by cardiac biomarkers elevation. The time from onset of symptoms to onset of reperfusion therapy was not recorded in the database. From observational studies in France and data from the CAPTIM and other randomized trials,[1,2] however, it is expected that the time gained by using PHT compared with in-hospital thrombolysis was ≈60 minutes. In addition, recent data from SAMU registries concur in showing that the time from initiation of PHT to hospital admission is ≈30 minutes,[13] suggesting a particularly beneficial effect of PHT when initiated within 3 hours of symptom onset. Likewise, the type of thrombolytic treatment used was not recorded in the database. At that time, accelerated tissue plasminogen activator was by far the most common treatment in France and was the sole treatment used for PHT; it is likely that the use of bolus thrombolytic therapy, as is currently the case in our

country, might even further improve the results of PHT.[20] The French system of primary care for emergencies is based on the use of the SAMU, which has extensive experience in terms of patient triage in the setting of prolonged chest pain. Therefore, our conclusions may not be directly applicable to other systems delivering PHT. Finally, because patients were included in the registry only when they reached the hospital, it cannot be excluded that a small percentage of the patients in the PHT group and those scheduled for other modes of reperfusion therapy might have died before being admitted to hospital. However, it must be remembered that 0 of the 419 patients randomized to the PHT arm of the CAPTIM trial died before hospital admission. In the 2003 fully comprehensive registry of the Paris SAMU, only 1 of 334 patients (0.3%) managed by the SAMU for AMI died before hospital admission. This patient, who had an evolving AMI caused by subacute stent thrombosis, died on his way to the catheterization laboratory for primary PCI; he had not received PHT (P.S., unpublished data).

Conclusions

The results of this nationwide prospective registry of patients admitted to intensive care units for AMI in November 2000 in France show that PHT therapy with liberal use of early angioplasty offers 1-year mortality results that are at least as satisfactory as those with primary coronary angioplasty. In patients treated very early (those admitted within 3.5 hours of onset of chest pain), PHT offers superior efficacy compared with any other mode of reperfusion therapy.

Acknowledgments

This study was supported by a grant from Laboratoires Aventis, Paris, France. We are indebted to all physicians in the participating centers, without whose collaboration this study would not have been possible, and to Christelle Cantet, for her technical assistance.

Disclosure

Drs Danchin, Blanchard, Hanania, Cambou, Guéret, and Lablanche were compensated by Aventis Paris for their participation in the steering committee of the USIC 2000 registry. Drs Boutalbi, Genès, and Vaur are full-time employees of Aventis, Paris, France.

References

1. Morrison LJ, Verbeek PR, McDonald AC, et al. Mortality and prehospital thrombolysis for acute myocardial infarction: a meta-analysis. *JAMA*. 2000;283:2686–2692.
2. Bonnefoy E, Lapostolle F, Leizorovicz A, et al, on behalf of the CAPTIM Study Group. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. *Lancet*. 2002;360:825–829.
3. Hanania G, Cambou JP, Guéret P, et al, for the USIC 2000 Investigators. Management and in-hospital outcome of patients with acute myocardial infarction admitted to intensive care units at the turn of the century: results from the French nation-wide USIC 2000 registry. *Heart*. In press.
4. Danchin N, Vaur L, Genès N, et al. Management of acute myocardial infarction in intensive care units in 1995: a nationwide French survey of practice and early hospital results. *J Am Coll Cardiol*. 1997;30:1598–1605.
5. Danchin N, Vaur L, Genès N, et al. Treatment of acute myocardial infarction by primary coronary angioplasty or intravenous thrombolysis in the "real world": one-year results from a nation-wide French survey. *Circulation*. 1999;99:2639–2644.
6. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*. 2003;361:13–20.
7. Every NR, Parisons LS, Hlatky M, et al, for the Myocardial Infarction Triage and Intervention Investigators. A comparison of thrombolytic therapy with primary coronary angioplasty for acute myocardial infarction. *N Engl J Med*. 1996;335:1253–1260.
8. Tiefenbrunn AJ, Chandra NC, French WJ, et al. Clinical experience with primary percutaneous transluminal coronary angioplasty compared with alteplase (recombinant tissue-type plasminogen activator) in patients with acute myocardial infarction: a report from the Second National Registry of Myocardial Infarction (NRMI-2). *J Am Coll Cardiol*. 1998;31:1240–1245.
9. GREAT Group. Feasibility, safety and efficacy of domiciliary thrombolysis by general practitioners. *BMJ*. 1992;305:548–553.
10. Steg PG, Bonnefoy E, Chabaud S, et al, for the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) Investigators. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. *Circulation*. 2003;108:2851–2856.
11. Boersma E, Maas AC, Deckers JW, et al. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet*. 1996;348:771–775.
12. Simes RJ, Topol EJ, Homes DR, et al. Link between the angiographic substudy and mortality outcomes in a large randomized trial of myocardial reperfusion: importance of early and complete infarct artery reperfusion. *Circulation*. 1995;91:1923–1928.
13. Sebbah JL. E-must Ile de France. *Rev SAMU*. 2003;25:420–427.
14. Andersen H, Nielsen T, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med*. 2003;349:733–742.
15. Hasdai D, Behar S, Wallentin L, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin: the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J*. 2002;23:1190–1121.
16. Loubeyre C, Lefèvre T, Louvard Y, et al. Outcome after combined reperfusion therapy for acute myocardial infarction, combining prehospital thrombolysis with immediate percutaneous coronary intervention and stent. *Eur Heart J*. 2001;22:1128–1135.
17. Juliard JM, Himbert D, Cristofini P, et al. A matched comparison of the combination of prehospital thrombolysis and standby rescue angioplasty with primary angioplasty. *Am J Cardiol*. 1999;83:305–310.
18. Rawles J. GREAT: 10-year survival of patients with suspected acute myocardial infarction in a randomised comparison of prehospital and hospital thrombolysis. *Heart*. 2003;89:563–564.
19. Widimsky P, Budesinsky T, Vorac D, et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction: final results of the randomized national multicentre trial: PRAGUE-2. *Eur Heart J*. 2003;24:94–104.
20. Llevadot J, Giugliano RP, Antman EM. Bolus fibrinolytic therapy in acute myocardial infarction. *JAMA*. 2001;286:442–449.

Impact of Prehospital Thrombolysis for Acute Myocardial Infarction on 1-Year Outcome: Results From the French Nationwide USIC 2000 Registry

Nicolas Danchin, Didier Blanchard, Philippe Gabriel Steg, Patrick Sauval, Guy Hanania, Patrick Goldstein, Jean-Pierre Cambou, Pascal Guéret, Laurent Vaur, Youcef Boutalbi, Nathalie Genès and Jean-Marc Lablanche
for the USIC 2000 Investigators

Circulation. 2004;110:1909-1915; originally published online September 27, 2004;
doi: 10.1161/01.CIR.0000143144.82338.36
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539