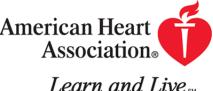


JOURNAL OF THE AMERICAN HEART ASSOCIATION



Implementation of Guidelines Improves the Standard of Care: The Viennese Registry on Reperfusion Strategies in ST-Elevation Myocardial Infarction (Vienna STEMI Registry)

Karim Kalla, Günter Christ, Ronald Karnik, Reinhard Malzer, Georg Norman, Herbert Prachar, Wolfgang Schreiber, Gerhard Unger, Helmut D. Glogar, Alfred Kaff, Anton N. Laggner, Gerald Maurer, Johannes Mlczoch, Joerg Slany, Heinrich S. Weber, Kurt Huber and for the Vienna STEMI Registry Group

Circulation 2006;113;2398-2405; originally published online May 15, 2006; DOI: 10.1161/CIRCULATIONAHA.105.586198

Circulation is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514

Copyright © 2006 American Heart Association. All rights reserved. Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circ.ahajournals.org/cgi/content/full/113/20/2398

Subscriptions: Information about subscribing to Circulation is online at http://circ.ahajournals.org/subsriptions/

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21202-2436. Phone 410-5280-4050. Fax: 410-528-8550. Email: journalpermissions@lww.com

Reprints: Information about reprints can be found online at http://www.lww.com/static/html/reprints.html

Coronary Heart Disease

Implementation of Guidelines Improves the Standard of Care

The Viennese Registry on Reperfusion Strategies in ST-Elevation Myocardial Infarction (Vienna STEMI Registry)

Karim Kalla, MD; Günter Christ, MD; Ronald Karnik, MD; Reinhard Malzer, MD; Georg Norman, MD; Herbert Prachar, MD; Wolfgang Schreiber, MD; Gerhard Unger, MD; Helmut D. Glogar, MD; Alfred Kaff, MD; Anton N. Laggner, MD; Gerald Maurer, MD; Johannes Mlczoch, MD; Joerg Slany, MD; Heinrich S. Weber, MD; Kurt Huber, MD; for the Vienna STEMI Registry Group

Background—The purpose of this study was to determine whether implementation of recent guidelines improves in-hospital mortality from acute ST-elevation myocardial infarction (STEMI) in a metropolitan area.

Methods and Results—We organized a network that consisted of the Viennese Ambulance Systems, which is responsible for diagnosis and triage of patients with acute STEMI, and 5 high-volume interventional cardiology departments to expand the performance of primary percutaneous catheter intervention (PPCI) and to use the fastest available reperfusion strategy in STEMI of short duration (2 to 3 hours from onset of symptoms), either PPCI or thrombolytic therapy (TT; prehospital or in-hospital), respectively. Implementation of guidelines resulted in increased numbers of patients receiving 1 of the 2 reperfusion strategies (from 66% to 86.6%). Accordingly, the proportion of patients not receiving reperfusion therapy dropped from 34% to 13.4%, respectively. PPCI usage increased from 16% to almost 60%, whereas the use of TT decreased from 50.5% to 26.7% in the participating centers. As a consequence, in-hospital mortality decreased from 16% before establishment of the network to 9.5%, including patients not receiving reperfusion therapy. Whereas PPCI and TT demonstrated comparable in-hospital mortality rates when initiated within 2 to 3 hours from onset of symptoms, PPCI was more effective in acute STEMI of >3 but <12 hours' duration.

Conclusions—Implementation of recent guidelines for the treatment of acute STEMI by the organization of a cooperating network within a large metropolitan area was associated with a significant improvement in clinical outcomes. (Circulation. 2006;113:2398-2405.)

Key Words: myocardial infarction ■ percutaneous coronary intervention ■ thrombolytic therapy ■ guidelines ■ mortality

Recently published American College of Cardiology (ACC)/American Heart Association (AHA) and European Society of Cardiology (ESC) guidelines^{1,2} recommend primary percutaneous coronary intervention (PPCI) as the preferred reperfusion strategy in ST-segment-elevation myocardial infarction (STEMI), if (1) first medical contact-to-balloon time or door-to-balloon time is <90 minutes; (2) the percutaneous coronary intervention (PCI)-related delay (door-to-balloon) compared with thrombolytic therapy (TT; door-to-needle) is <60 minutes; (3) the interventionist is experienced (performs >75 PCI cases per year); and (4) the patient is treated in a high-volume center (one that performs

>36 PPCI cases per year), respectively. Furthermore, highrisk patients, such as patients in cardiogenic shock or with Killip class ≥3, and patients with uncertain diagnoses should preferably undergo angiography with a view to PPCI, as should patients with absolute contraindications to TT.

Editorial p 2377 Clinical Perspective p 2405

In the community at large, however, times from first medical contact to balloon of up to 120 minutes and more^{3,4} are frequent and present in the majority. Moreover, even in the developed world, PPCI can only be offered to 20% to

Received August 31, 2005; revision received January 30, 2006; accepted March 10, 2006.

Correspondence to Kurt Huber, Director, 3rd Medical Department, Cardiology and Emergency Medicine, Wilhelminenhospital, Montleartstrasse 37, A-1160 Vienna, Austria. E-mail kurt.huber@wienkav.at

© 2006 American Heart Association, Inc.

From Wilhelminenhospital (K.K., G.U., K.H.), 3rd Medical Department, Cardiology and Emergency Medicine; Department of Cardiology (G.C., H.D.G., G.M.), Medical University Vienna; Krankenhaus Rudolfstiftung (R.K., J.S.), 2nd Medical Department, Cardiology; Ambulance Services Vienna (R.M., A.K.); Sozialmedizinisches Zentrum Ost (G.N., H.S.W.), 1st Medical Department, Cardiology; Krankenhaus Lainz (H.P., J.M.), 4th Medical Department, Cardiology; and Department of Emergency Medicine (W.S., A.N.L.), University of Medicine, Vienna, Austria.

30% of the patients presenting with acute STEMI, primarily because of regional logistical constraints and the limited availability of catheterization facilities. Furthermore, among patients treated with PPCI, usually fewer than 15% can be treated within 2 hours of onset of pain.⁵

TT is preferred in patients with acute STEMI if an invasive strategy cannot be offered at all or if it is anticipated that delays before PPCI would be unacceptably long.^{1,2} From a clinical perspective, TT is effective until 12 hours from onset of symptoms, with highest success rates, however, within the first 2 to 3 hours after symptom onset, when the occluding fresh thrombus is more likely to be dissolved pharmacologically.⁶ Accordingly, mortality reduction as a benefit of reperfusion therapy is greatest in the first 2 to 3 hours after symptom onset, most likely as a consequence of myocardial salvage, irrespective of the reperfusion strategy.^{7,8} After this very early period, the impact on mortality is much reduced, and time to reperfusion is far less critical. In this situation, opening the infarct-related artery is the main goal of reperfusion, and PPCI is believed to be the more effective method.⁷

In general, longer times to treatment are inversely related to mortality with both TT9 and PPCI.^{10,11} At present, interventional cardiologists frequently prefer PPCI irrespective of the times to balloon inflation; such an approach ignores the relationship between time to treatment and myocardial salvage within the first few hours of myocardial infarction. On the other hand, emergency department physicians often prefer pharmacological reperfusion despite the availability of an open catheterization laboratory within the recommended time frames, which does not take into account the superiority of PPCI in terms of higher reperfusion and lower intracerebral bleeding rates. With regard to the hard clinical end points, eg, in-hospital death or mortality after 30 days, the 2 strategies, particularly in acute STEMI of less than 2 to 3 hours' duration, are comparable.^{12,13}

In patients presenting within the first 2 to 3 hours of STEMI, what is critical is not so much the actual strategy used but the rapidity of its delivery. Moreover, because $\approx 25\%$ to 40% of patients worldwide who present with clinical signs of acute STEMI do not receive reperfusion therapy at all, ¹⁴ a formidable challenge in the contemporary era is to extend the use of reperfusion therapies to all who are likely to benefit.

To improve the utilization of STEMI therapy in Vienna, Austria, and to determine the effect of implementation of guidelines on therapeutic efficacy in this metropolitan area, in March 2003, an initiative with the goal of optimizing the organization of reperfusion strategies was started. This was based on (1) the then-recommended time intervals, which have subsequently been published, 1,2 and (2) the varying clinical status of individuals presenting with myocardial infarction. For this purpose, we created uniformity among catheterization laboratories by the implementation of a central triage network via the Viennese Ambulance System (VAS) in conjunction with recommendations to initiate TT, either in-hospital or before arrival at the hospital (the latter starting in March 2004), if PPCI could not be offered in a timely fashion, particularly in the case of patients with a duration of symptoms of <2 hours. At the same time, a prospective registry was established for control and quality assurance purposes.

Methods

Patient Population of the Registry

Data presented reflect the first 1053 consecutive patients with acute STEMI who were admitted to 1 of the 5 participating high-frequency (>400 PCI cases/year, >40 PPCI cases/year) cardiology departments either by the VAS (approximately two thirds of the total patients) or who came directly to the respective departments (usually to the emergency room [ER]) by private transport (approximately one third). After a first medical contact, diagnosis of acute STEMI was confirmed by clinical signs (characteristic chest pain) and the typical findings on a 12-lead ECG.¹

Comparison Population

Baseline characteristics of patients admitted with acute myocardial infarction who were treated in the 5 participating centers before the network was created were retrospectively analyzed from official health statistics from insurance companies concerning age, sex distribution, and infarct location, respectively.¹⁵ Proportions of patients with acute myocardial infarction presenting in shock in the participating centers in the years 2002 and 2004 were evaluated from the official "Coronary Angiography and PCI Reports" for Austria.^{16,17}

Optimization of Reperfusion Strategies

At the end of 2002, in Vienna (1.8 million inhabitants), only 1 catheterization laboratory (at the Department of Cardiology, University of Vienna) offered a 24-hour PPCI service on a routine basis (on-call) for patients with acute STEMI. In addition, during official working hours (ie, Monday to Thursday 7:30 AM to 4:00 PM, Friday 7:30 AM to 1:00 PM), 4 other high-frequency nonacademic centers with catheterization facilities were available for PPCI but had not coordinated their activities. From 4:00 PM (Monday to Thursday) until the next morning and from Friday 1:00 PM until Monday morning, PPCI was occasionally performed in these centers, but this was dependent on the level of risk and clinical status of the individual patient and also on local circumstances (eg, whether an experienced interventionist was on duty). This situation was profoundly reorganized by the implementation of (1) central triage for STEMI patients by the VAS; (2) a second catheterization laboratory open at night (Monday to Friday) by use of a rotation principle between the 4 nonacademic hospitals (on weekends [Friday afternoon to Monday morning], only 1 catheterization center was active during this first network solution); and (3) prehospital or in-hospital TT if acute PPCI was unlikely to be offered within the recommended time intervals, respectively.

Activities of the VAS

The primary diagnosis of acute STEMI and triage of patients to the respective reperfusion method, either PPCI or prehospital TT, was performed by physicians of the VAS who had been trained in the diagnosis of acute STEMI, for triage to the fastest available reperfusion method and for organization of transfer to the nearest catheterization center.

Reperfusion Strategies

In general, reperfusion therapy was given to patients with characteristic symptoms of STEMI of <12 hours' duration at presentation and with associated ST-segment elevation in 2 or more leads or left bundle-branch block on their first ECG. PPCI was offered to patients with acute STEMI if time from first medical contact (after having established the diagnosis) until first balloon dilation of the infarct-related coronary artery was estimated to be within 90 minutes. Antithrombotic strategies during PPCI included aspirin (250 mg IV), unfractionated heparin (UFH; 70 U/kg, without a maximum dose), clopidogrel (300 or 600 mg loading dose at discretion of the interventionist), and a glycoprotein (GP) IIb/IIIa inhibitor (in 70% of the cases), either abciximab (bolus plus infusion) or eptifibatide (double bolus plus infusion), respectively. GP IIb/IIIa inhibitors were used in the majority of patients (97%) in the catheterization laboratory and were initiated only occasionally during the organization

TABLE 1. Patient Demographics

	All Patients	PPCI	TT	No Reperfusion	P*
Number (%)	1053 (100)	631 (59.9)	281 (26.7)	141 (13.4)	
Women, %	28.4	27	27	37	0.021
Anterior wall infarction, %	51.1	50.1	49	60.2	0.035
Age, y, mean±SD	$61.8\!\pm\!13.5$	61.8 ± 13.5	$60.8 \!\pm\! 13.0$	68 ± 14	< 0.001
Age $>$ 75 y, %	20.5	17.3	19.2	32.6	< 0.001
Cardiogenic shock, %	12	11.8	12.7	11.4	0.93

^{*}P values are calculated between reperfused (PPCI and TT) and nonreperfused patients. No statistical significance could be demonstrated between reperfusion groups.

phase for PPCI in the emergency room but never prehospital. All patients received stents during PPCI (90% use of bare-metal stents).

If, however, the anticipated delay to PPCI was expected to exceed 90 minutes, patients received TT, either prehospital in the ambulance or in-hospital in the ER. Patients presenting more than 2 to 3 hours after onset of pain and those with uncertain diagnosis, high age, increased bleeding risk, and perceived contraindications against TT were treated with PPCI even if time to balloon dilation was prolonged.

Prehospital TT was performed by use of tenecteplase in combination with UFH (60 U/kg body weight; maximum 4000 U) and was preferably offered to patients with anterior wall infarction and infarct duration of <2 hours. After initiation of prehospital TT, patients were immediately transferred to an open catheterization laboratory. In nonresponders to TT, as diagnosed 60 minutes after initiation of TT, rescue PCI was performed immediately. Failed TT was defined as ST-segment resolution of <50% 60 minutes after initiation of TT or ongoing chest pain. In responders to TT, it was left to the discretion of the interventional cardiologist whether to perform either immediate PCI ("facilitated PCI") or coronary angiography with or without PCI on a routine basis between days 1 and 5 after TT. In-hospital TT was performed with tenecteplase, alteplase (accelerated regimen), or reteplase according to common dose regimens.6 Aspirin and UFH or low-molecular-weight heparin but not clopidogrel were used as combined therapy. After in-hospital TT, nonresponders were transferred to an open catheterization center, and those in high-risk situations (eg, anterior infarctions, signs of heart failure, and shock) were given preference for transfer.

Data Collection and Statistics

To collect, audit, and statistically evaluate important clinical variables (patient characteristics, risk markers, ECG parameters, time intervals, therapeutic approaches, and clinical follow-up during in-hospital stay), a specific protocol had to be completed on all patients. Individual patient data were handled in a blinded fashion, and the registry was performed according to the Helsinki criteria. All protocols were sent for further evaluation to a data collection and statistic core laboratory (Wilhelminenhospital).

For calculation of the influence of time on in-hospital mortality for the different reperfusion methods, patients were divided into 3 groups according to different time intervals between onset of pain and initiation of the respective reperfusion strategy (from start of infusion of the thrombolytic agent or first balloon dilation), ie, up to 2 hours, 2 to 6 hours, and 6 to 12 hours, respectively. ANOVA and t tests were used to evaluate differences in continuous variables, and χ^2 tests were used for categorical variables. A probability value of <0.05 was considered to be statistically significant. All calculations were performed with the SPSS 11.5 for Windows XP Professional statistical system (SPSS Inc, Chicago, Ill).

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

Results

Patient Population

Table 1 summarizes the demographics of patients according to the reperfusion strategy used. Of the total population, 28.4% of patients were women. Women accounted for 27% in each reperfusion group, whereas among patients who did not receive reperfusion therapies, the proportion of women increased to 37% (P=0.021). About half of the patients had anterior wall infarction at presentation. The percentage of anterior wall infarctions in the population without reperfusion therapy was higher (60.2%; P=0.035). Mean age was 61.8 years for the total population, was similar among PPCI (61.8) years) and TT (60.8 years) patients, but was significantly higher (68 years) in the nonreperfused group (P < 0.001). The proportion of elderly individuals (those aged >75 years) was 20.5% for the entire patient population, with no difference between PPCI (17.3%) and TT (19.2%) patients, but increased to 32.6% (P<0.001) in patients not receiving any reperfusion strategy. The frequency of cardiogenic shock at presentation was similar for all groups.

Changes in Reperfusion Strategies, 2002 to 2004

On the basis of official health statistics, in 2002, 34% of patients presenting with acute STEMI at 1 of the 5 participating centers did not receive any reperfusion therapy. Accordingly, at that time, reperfusion therapy was offered to 66% of the patients, but only 16% received PPCI, whereas 50% were treated with in-hospital thrombolysis. Prehospital thrombolysis was not performed until March 2004, because the benefits of the prehospital approach of pharmacological reperfusion in an urban setting with short transportation delays had not been previously accepted by the majority of cardiologists in the area.¹⁸ Another factor contributing to the lower use of PPCI in 2002 was a lack of open catheterization laboratories, particularly on weekends and nights, when only 1 center was active on a routine basis. In addition, patients with acute STEMI were frequently transferred to the nearest cardiology department irrespective of the availability of facilities for cardiac catheterization and were either treated with TT, occasionally received PPCI on an individual nonroutine basis, or were transferred for PPCI to an open invasive center. Accordingly, time delays until the patient was finally treated with mechanical reperfusion frequently exceeded 2 to 3 hours after diagnosis. After reorganization of reperfusion strategies in Vienna, the percentage of patients without reperfusion therapy fell to 13.4%, the proportion of patients receiving any reperfusion strategy increased to 86.6%, the proportion of patients treated with TT was reduced to 26.7%, and the use of PPCI increased to \approx 60% (Figure 1). The reasons for not offering any reperfusion

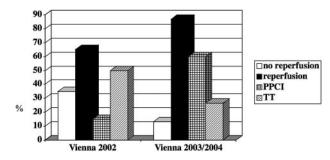


Figure 1. Reperfusion strategies in patients with acute STEMI in Vienna: comparison of data generated before and after the implementation of recent guidelines in the participating hospitals.

strategy to $\approx 13\%$ of the patients was a combination of different factors, eg, extended delay between the onset of chest pain and presentation, advanced age, multiple comorbidities, and related contraindications in patients with myocardial infarctions.

Time Intervals and Reperfusion Strategies

The mean time from symptom onset to arrival at hospital was 180 minutes (Table 2). The components of the total delay were (1) the patients' delay until call for medical help (roughly 120±150 minutes), (2) the time from call until first medical contact (including 12-lead ECG and confirmation of the diagnosis; 20±30 minutes), and (3) the transportation delay (20 minutes). Only half of the patients arrived at a hospital within the first 2 hours after onset of pain. In the PPCI group, the mean time from onset of pain to treatment (first balloon dilation) was 258±168 minutes, whereas it was 120±108 minutes in patients treated with TT (onset of pain until start of infusion of the thrombolytic agent; P < 0.001; Table 2). The relatively short intervals seen with TT can be explained in part by the selection of patients treated with TT (anterior wall infarction in the majority of patients with infarct duration of <2 hours). Onset of pain to TT was 76 minutes in the patients receiving prehospital TT (n=34;

TABLE 2. Delay Times

	Delay Times, min			
	All Patients	PPCI	TT	No Treatment
Onset of pain to hospital arrival	180±156	174±150	132±120	252±222
Onset of pain to reperfusion*		258±168	120±108	
First contact/door to cath lab (arrival)		52±44		
Cath lab to balloon		$31\!\pm\!23$		
First contact/door to balloon (PPCI)		81±51		
First contact/door to needle (TT)			17±13	

Cath lab indicates catheterization laboratory. Values are mean ± SD.

12.1% of patients referred to TT) but 162 minutes in in-hospital TT (n=247; 87.9%; P<0.001). About half of the patients (50.5%) treated with TT received therapy within 2 hours after symptom onset (Figure 2). In contrast, only 14.6% of the patients receiving PPCI could be treated within 2 hours of symptom onset.

First medical contact–to-balloon time (by VAS physicians) or door-to-balloon time (by ER physicians) was 81 ± 51 minutes and consisted of the time interval between first medical contact and arrival in the catheterization laboratory (52 ± 44 minutes) and the time interval from arrival in the catheterization laboratory to first balloon inflation (31 ± 23 minutes). In patients treated with prehospital or in-hospital TT, first medical contact-to-needle time was identical (17 ± 13 minutes each). Coronary angiography was performed in 91% of the patients and was waived only in rare cases (eg, in very old patients without postinfarction angina and with small infarctions).

In $\approx 50\%$ of patients, immediate PCI was performed, either as rescue PCI in nonresponders (25%) or as facilitated PCI in responders. Forty-one percent underwent diagnostic angiography on a routine basis during days 1 to 5 of the hospital stay. PCI and stent implantation (90% of which consisted of bare-metal stents) was performed in 85% of the patients undergoing acute or elective angiography. Early coronary bypass grafting was performed in 4.4% of patients after diagnostic angiography.

In-Hospital Mortality

As summarized in Table 3, in-hospital mortality was 9.5% for the entire patient population, including patients without reperfusion therapy. Although patients with PPCI had a similar mortality rate compared with patients treated with TT (8.1% and 8.2%, respectively), the mortality rate for patients without reperfusion therapy was significantly increased (18.4%; P<0.01). In-hospital mortality rates were lowest in patients treated within 2 hours of symptom onset; although the differences were not statistically significant, there was a trend in favor of TT over PPCI (PPCI 7.8%, TT 5.1%; P=0.37); however, with increasing time intervals from onset of symptoms, there appeared to be an increasing survival benefit from PPCI over TT (Figure 3).

Female sex, increasing age, and presentation in shock were independent predictors (univariate analysis) of higher inhospital mortality rates in both reperfusion groups, as well as in patients who did not receive reperfusion therapy (Table 3). Women had almost double the mortality rate as men undergoing PPCI, although this did not reach statistical significance (P=0.18), whereas the mortality rate in patients treated with TT was almost 3 times higher in women than in men (P < 0.005). Furthermore, women were older than men $(67.4\pm14.4 \text{ versus } 59.6\pm12.5 \text{ years, mean}\pm\text{SD}; P<0.01),$ had a higher incidence of shock at presentation (14.1% versus 11.2%; P<0.01), and had a tendency for a more prolonged time interval between onset of pain to treatment in both reperfusion groups, which was significant only for patients undergoing TT (PPCI 264±168 versus 252±2.8 minutes, P=0.553; TT 180±138 versus 144±102 minutes, P=0.02;

^{*}Reperfusion means start of infusion of the thrombolytic agent or first balloon dilation.

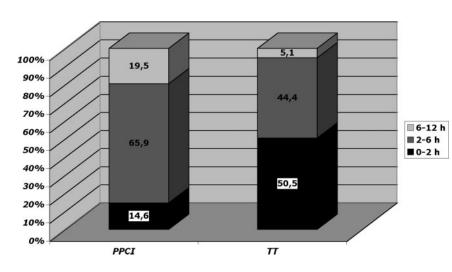


Figure 2. Time to treatment and use of reperfusion strategies. PPCI could only be offered to 14.6% of patients within the first 2 hours after symptom onset, whereas it was offered to 50.5% of patients undergoing TT.

mean±SD). No difference was observed for infarct location between women and men.

The higher mortality rates in women were related to their more adverse risk profile (age, incidence of shock, and time to treatment), as was confirmed by multivariable analysis that demonstrated that female gender did not emerge as an independent predictor of in-hospital death (Table 4). Independent predictors of in-hospital mortality were shock, age, time to reperfusion, and infarct location. Patients who were 60 years old or younger had the lowest in-hospital mortality, followed by patients in the age group 61 to 75 years and patients older than 75 years (Table 3).

In patients without clinical signs of shock, mortality was in general low, irrespective of the nature of the reperfusion strategy. In patients without cardiogenic shock at presentation, in-hospital mortality was significantly lower for patients treated with TT (2.1% in the TT group, 2.9% in the PPCI group; P=0.038).

Figure 4 depicts the impact of combining the 2 most important risk predictors, shock and age, for in-hospital mortality in all patients (including nonreperfused patients), as well as for patients reperfused by means of PPCI or TT,

TABLE 3. In-Hospital Mortality

	In-Hospital Mortality, %			
	All Patients	PPCI	TT	No Reperfusion
Total	9.5	8.1	8.2	18.4
Men	7.4	6.5	5.4	16.9
Women	14.7	12.3	15.8	21.2
Р	< 0.001	0.18	0.005	0.525
Age, y				
<60	3.1	2.4	2.1	11.6
61 to 75	10.5	10.1	11.8	10
>75	23.6	22.1	18.2	33.3
Р	< 0.001	< 0.001	< 0.001	0.018
Shock vs no shock				
Shock	50.8	47.3	48.6	73.3
No shock	3.9	2.9	2.1	12.2
P	< 0.001	< 0.001	< 0.001	< 0.001

respectively. In all groups, the combination of increasing age with the presence of cardiogenic shock was associated with the highest mortality rates.

Discussion

Enhanced delivery of reperfusion strategies based on the development of a comprehensive regional network, the coordinated transfer of patients to the nearest open catheterization facilities, and the use of the fastest available reperfusion strategy in patients with STEMI of less than 2 to 3 hours led to an impressive reduction of in-hospital mortality in patients presenting with acute STEMI, down to 9.5% compared with official in-hospital mortality statistics in patients with acute STEMI in 2002 (16%) in the cardiology centers participating in the registry.¹⁵ Three major factors might have influenced the results: (1) the increase in the use of PPCI from \approx 16% to 60%; (2) the use of TT in the setting of nonavailability of prompt PPCI, especially in patients with myocardial infarction of short duration; and (3) a remarkable and gratifying reduction in the number of patients who did not receive any form of reperfusion therapy from $\approx 34\%$ to 13%, respectively.

In patients treated early after onset of pain (within 2 to 3 hours), no difference could be demonstrated between TT and

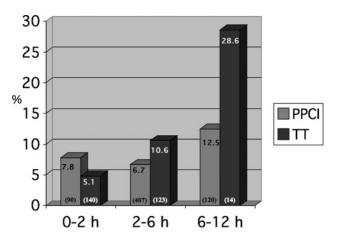


Figure 3. Influence of time to treatment on in-hospital mortality. Within the first 2 hours after onset of pain, TT showed a tendency for lower mortality rates than PPCI. This relation was reversed in the later time categories. Numbers in parentheses represent patient numbers in the different treatment groups.

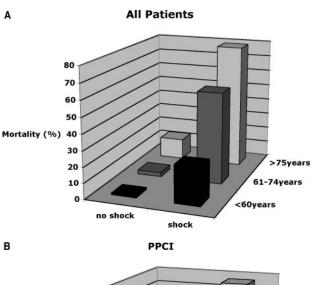
TABLE 4. Multivariable Analysis of Predictors of Mortality

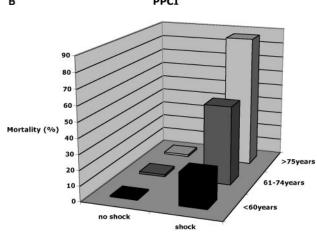
Variables	Р	OR	
Shock	< 0.001	54.21	
Age	< 0.001	11.05	
Pain to reperfusion time	0.05	1.23	
Infarct location	0.036	0.474	
Gender	0.855	0.932	

PPCI, again showing the similarity of the 2 reperfusion strategies in terms of in-hospital mortality in early STEMI, as has been demonstrated elsewhere 12,13 (Figure 5): Similar to the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) trial, we were able to demonstrate a trend in favor of TT in patients when treatment was initiated within 2 hours of onset of pain.¹² Possible explanations for this finding are the relatively low number of patients receiving PPCI within 2 hours of symptom onset compared with patients treated with TT or, on the other hand, that the prothrombotic milieu in the early phase of myocardial infarction^{19,20} might have interfered with optimal results from mechanical reperfusion alone. Whether early initiation of GP IIb/IIIa blockers (prehospital or in the ER) might decrease these prothrombotic mechanisms and therefore help to optimize the local situation for PPCI, as assumed by others, 21,22 is still a matter of debate, but this was not part of our routine reperfusion strategy. After >3 hours of onset of pain, PPCI was significantly more successful than TT, thus indicating the role of an open infarctrelated artery for clinical outcome.7

Ninety-one percent of patients initially treated with TT received coronary angiography within the hospital stay (50% within 1 day of admission, 41% later), either as rescue PCI in nonresponders to TT, or in responders, immediately as facilitated PCI or later as elective PCI, between day 1 and 5 after the acute event. This proportion of early coronary angiography after initial TT is higher than in most published trials. Therefore, it was not just TT that influenced the clinical outcome but rather a synergistic combination of TT in connection with early angiography followed by mechanical reperfusion in many patients.

The Viennese model (a partial rotation system between hospitals for nonofficial catheterization working hours) has several advantages: the permanent availability of well-trained interventionists for nighttime and weekend duty, the higher experience of participating centers because of a higher case load per center, and a higher likelihood of available critical care unit beds and thus the avoidance of early retransfer of patients to their home hospitals in a potentially critical phase of disease, which often is necessary if these facilities cannot be offered.² The organization of a network to optimize early diagnosis and treatment of patients with acute STEMI might also have beneficial implications for the future, because other prehospital treatment options could easily be implemented as soon as these "facilitating" methods have been shown to be beneficial for patients referred for PPCI, eg, the use of prehospital GP IIb/IIIa blockers and/or high-dose clopidogrel.8





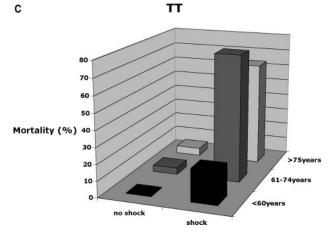


Figure 4. A through C, Predictors of in-hospital mortality: relationship of age, shock, and mortality. Patients with increasing age and signs of shock exhibited the highest mortality rates in all patient groups.

Study Limitations

This prospective registry is subject to all the limitations of registry studies as opposed to randomized trials; however, one benefit is that the results are a reflection of therapeutic outcomes in the entire community and as such are more generalizable than those from the more restricted population that is entered into randomized trials. Accordingly, it is not possible to draw firm conclusions with respect to the dem-

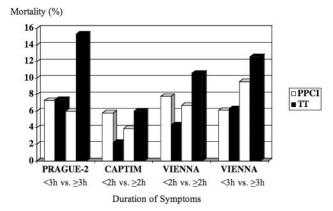


Figure 5. In-hospital mortality according to time delays: comparison between the Vienna registry and the CAPTIM and PRAGUE-2 (PRimary Angioplasty after transport of patients from General community hospitals to catheterization Units with/without Emergency thrombolytic infusion) trials.

onstrated differences in in-hospital mortality between the 2 reperfusion strategies.

The study lacks an ideal control group: Although the registry was performed prospectively, data from 2002 have been evaluated retrospectively and are based mainly on the official health statistics of public insurance companies. However, baseline variables using these databases to compare patients of the 5 participating centers with the diagnosis of acute myocardial infarction between 2002 and 2004 revealed similarity with respect to patient's age, proportion of women (trend for increase), and infarct location, respectively.¹⁵ Moreover, as shown in the annual "Coronary Angiography and PCI Reports for Austria," the proportion of patients with acute STEMI presenting in shock at hospital admission was similar (trend for increase) in the years 2002 and 2004 for the 5 participating Viennese centers. 16,17 Adjunctive medical therapy with PPCI or TT was not changed during the past years and was related to international guidelines,24 although we did not record these data specifically in the database. Therefore, the only significant change between the patient cohorts treated before and after implementation of guidelines by the creation of a network was the optimization and organization of reperfusion strategies, and it is likely that this is the major factor responsible for the improvement in outcomes, although we cannot entirely discount the impact of changes in other unmeasured variables on outcome.

Conclusions

In summary, the implementation of recent guidelines for the treatment of acute STEMI in a metropolitan area by means of a network has led to a significant reduction of in-hospital mortality. When patients were treated in the early phase of disease (within 2 to 3 hours), in-hospital mortality did not differ between the 2 presently available reperfusion strategies, PPCI or TT. However, if reperfusion therapy was initiated later than 3 hours after onset of symptoms, PPCI appeared to be the method of choice. Besides offering the fastest available reperfusion method to patients with STEMI of short duration, the reduction in the number of patients not receiving reperfusion at all might have had the strongest influence on the results. These results serve as a reinforce-

ment of the guidelines themselves and as a benchmark for the benefits of their implementation.

Acknowledgments

The registry was planned and initiated under the auspices of responsible health politicians of the City of Vienna. Special thanks go to Dr Elisabeth Pittermann-Höcker (Executive City Councilor for Public Health and Social Affairs in Vienna) and Dr. Ludwig Kaspar (Director of the Wiener Krankenanstaltenverbund) for their important contributions.

Disclosures

None.

References

- Antman EM, Anbe DT, Armstrong P, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner F, Lamas GA, Mullany CJ, Ornato J, Pearle DL, Sloan MA, Smith SCJ. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: executive summary. *Circulation*. 2004;110:588-636.
- Silber S, Albertsson P, Aviles F, Camici PG, Colombo A, Hamm CW, Jorgensen E, Marco J, Nordrehaug J-E, Ruzyllo W, Urban P, Stone GW, Wijns W; the Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Guidelines for percutaneous coronary interventions. Eur Heart J. 2005;26:804–847.
- Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, Abilgaard U, Pedersen F, Madsen JK, Grande P, Villadsen AB, Krusell LR, Haghfelt T, Lomholt P, Husted SE, Vigholt E, Kjaergard HK, Mortensen LS; for the DANAMI-2 Investigators. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med. 2003;349:733–742.
- Nallamothu BK, Bates ER, Herrin J, Wang Y, Bradley EH, Krumholz HM. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. Circulation. 2005;111:761–767.
- De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation*. 2004;109:1223–1225.
- Huber K, Maurer G. Thrombolytic therapy in acute myocardial infarction. Semin Thromb Haemost. 1996;22:12–23.
- Gersh BJ, Stone GW, White HD, Holmes DR Jr. Pharmacological facilitation of primary percutaneous coronary intervention for acute myocardial infarction: is the slope of the curve the shape of the future? *JAMA*. 2005;293:979–986.
- Huber K, De Caterina R, Kristensen SD, Verheugt FWA, Montalescot G, Badimon Maestro L, Van de Werf F. Prehospital reperfusion therapy: a strategy to improve therapeutic outcome in patients with ST-elevation myocardial infarction. *Eur Heart J.* 2005;26:2063–2074.
- Newby KL, Rutsch WR, Califf RM, Simoons ML, Aylward PE, Armstrong PW, Woodlief LH, Lee KL, Topol E, Van de Werf F; GUSTO-1 Investigators. Time from symptom onset to treatment and outcomes after thrombolytic therapy. J Am Coll Cardiol. 1996;27:1646–1655.
- Antoniucci D, Valenti R, Migliorini A, Moschi G, Trapani M, Buonamici P, Cerisano G, Bolognese L, Santoro GM. Relation of time to treatment and mortality in patients with acute myocardial infarction undergoing primary coronary angioplasty. Am J Cardiol. 2002;89:1248–1252.
- De Luca G, Suryapranata H, Zijlstra F, van't Hof AW, Hoorntje JC, Gosselink AT, Dambrink JH, de Boer MJ. Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. J Am Coll Cardiol. 2003;42:991–997.
- 12. Bonnefoy E, Lapostolle F, Leizorovicz A, Steg G, McFadden EP, Dubien PY, Cattan S, Boullenger E, Machecourt J, Lacroute JM, Cassagnes J, Dissait F, Touboul P; for the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) Study Group. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomized study. *Lancet*. 2002;360:825–829.
- Widimsky P, Budesinsky T, Vorac D, Groch L, Zelizko M, Aschermann M, Branny M, Stasek J, Formanek P; on behalf of the PRAGUE Study Group Investigators. 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.
- Carruthers KF, Dabbous OH, Flather MD, Starkley I, Jacob A, Macleod D, Fox KA; for the GRACE Investigators. Contemporary management of acute

- coronary syndromes: does the practice match the evidence? The Global Registry of Acute Coronary Events (GRACE). *Heart*. 2005;91:290–298.
- Weber H, Rieder A, Allikmets C, Haidinger G. Akute Herzinfarkte in Wien 2002 (Aus dem Wiener Herzinfarktbericht 2004). J Kardiol. 2006;13:131–140.
- Mühlberger V, Barbieri V, Pachinger O. Koronarangiographie und PCI in Österreich 2004. J Kardiol. 2006;13:1–12.
- Mühlberger V, Glogar D, Klein W, Leisch F, Mlczoch J, Probst P, Raudaschl G, Sochor H, Pachinger O. Koronarangiographie und PCI in Österrreich im Jahr 2002. *J Kardiol*. 2003;10:496–502.
- Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: a meta-analysis. *JAMA*. 2000;283:2686–2692.
- Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of coronary artery disease and the acute coronary syndromes (part I). N Engl J Med. 1992;326:242–250.
- Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of coronary artery disease and the acute coronary syndromes (part II). N Engl J Med. 1992;326:310–318.
- Gyöngyösi M, Domanovits H, Benzer W, Haugk M, Heinisch B, Sodeck G, Hödl R, Gaul G, Bonner G, Wojta J, Laggner A, Glogar D, Huber K.

- Use of abciximab prior to primary angioplasty in STEMI results in early recanalization of the infarct-related artery and improved myocardial tissue reperfusion: results of the Austrian multicenter randomized ReoPro-BRIDGING Study. *Eur Heart J.* 2004;25:2125–2133.
- Montalescot G, Borentain M, Payot L, Collet JPH, Thomas AC. Early vs late administration of glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction: a meta-analysis. *JAMA*. 2004;292:362–366.
- 23. Danchin N, Blanchard D, Steg PG, Sauval P, Hanania G, Goldstein P, Cambou J-P, Gueret P, Vaur L, Boutalbi Y, Genes N, Lablanche J-M; for the USIC 2000 Investigators. Impact of prehospital thrombolysis for acute myocardial infarction on 1-year outcome: results from the French Nationwide USIC 2000 Registry. Circulation. 2004;110:1909–1915.
- 24. Van de Werf F, Ardissino D, Betriu A, Cokkinos DV, Falk E, Fox KA, Julian D, Lengyel M, Neumann FJ, Ruzyllo W, Thygesen C, Underwood SR, Vahanian A, Verheugt FWA, Wijns W; for the Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. Management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2003;24:28–66.

CLINICAL PERSPECTIVE

The VIENNA-STEMI Registry included >1000 consecutive patients with acute ST-elevation myocardial infarction (STEMI) who received 1 of 2 reperfusion strategies, either primary percutaneous coronary intervention (PCI) or thrombolytic therapy. Choice of reperfusion strategy was based on the then-discussed European PCI guidelines (discussed in 2003 to 2004 but only published in 2005) and therefore offers a first clue to the clinical impact of the implementation of these guidelines in a "real world" setting. Creating a network with the goal of offering an increased number of patients the fastest available reperfusion method led to a significant improvement in clinical outcome. Moreover, it could be demonstrated that the time from onset of symptoms to either of the therapeutic strategies matters and that thrombolytic therapy (preferably before arrival at the hospital) should not be withheld if primary PCI cannot be offered in a timely manner (within 90 minutes of first medical contact), especially in myocardial infarctions of <3 hours' duration.