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Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction

Final results of the randomized national multicentre trial—PRAGUE-2

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KEYWORDS
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thrombolysis;
long distance transport;
coronary intervention;
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stent

Background Primary percutaneous coronary intervention (PCI) is shown to be the most effective reperfusion strategy in acute myocardial infarction. The aim of this multicentre national randomized mortality trial was to test whether the nationwide change in treatment guidelines (transportation of all patients to PCI centres) was warranted.
Methods The PRAGUE-2 study randomized 850 patients with acute ST elevation myocardial infarction presenting within <12 h to the nearest community hospital without a catheter laboratory to either thrombolysis in this hospital (TL group, n = 421) or immediate transport for primary percutaneous coronary intervention (PCI group, n = 429). The primary end-point was 30-day mortality. Secondary end-points were: death/reinfarction/stroke at 30 days (combined end-point) and 30-day mortality among patients treated within 0–3 h and 3–12 h after symptom onset. Maximum transport distance was 120 km.
Results Five complications (1.2%) occurred during the transport. Randomization–balloon time in the PCI group was 97±27 min, and randomization–needle time in the TL group was 12±10 min. Mortality at 30 days was 10.0% in the TL group compared to 6.8% mortality in the PCI group ($P = 0.12$, intention-to-treat analysis). Mortality of 380 patients who actually underwent PCI was 6.0% vs 10.4% mortality in 424 patients who finally received TL ($P<0.05$). Among 299 patients randomized >3 h after the onset of symptoms, the mortality of the TL group reached 15.3% compared to 6% in the PCI group ($P<0.02$). Patients randomized within <3 h of symptom onset (n = 551) had no difference in mortality whether treated by TL (7.4%) or transferred to PCI (7.3%). A combined end-point occurred in 15.2% of the TL group vs 8.4% of the PCI group ($P<0.003$).
Conclusions Long distance transport from a community hospital to a tertiary PCI centre in the acute phase of AMI is safe. This strategy markedly decreases mortality in patients presenting >3 h after symptom onset. For patients presenting within <3 h of symptoms, TL results are similar results to long distance transport for PCI.

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Introduction

Direct coronary angioplasty as the primary reperfusion therapy for acute myocardial infarction was first described by Meyer[1] and Hartzler[2] in 1982–3. Ten years later three randomized studies showed the superiority of primary angioplasty over thrombolysis when used within the same period after onset of symptoms.[3–5] This was also confirmed by a meta-analysis of additional trials.[6] Currently there is no doubt that primary percutaneous coronary intervention (primary PCI) results in markedly lower in-hospital mortality[7–9] and decreased risk of reinfarction and stroke.[3–10] However, the use of primary PCI as the treatment of choice for all patients with acute myocardial infarction and ST segment elevations has not become routine. The explanation is complex: difficulties in the logistics of such an approach, large variation in PCI results between high- vs low-volume centres[9,11] and the possible deleterious effects of substantial treatment delay on myocardial salvage and resulting left ventricular function.[12–14]

The safety and feasibility of interhospital transportation of patients with acute myocardial infarction presenting initially to smaller hospitals without PCI facilities to the tertiary PCI centres was investigated by the LIMI study in the Netherlands[15] and by the PRAGUE-1 study in the Czech Republic.[16] Both these studies clearly proved the safety and feasibility of the transport and both had the same direction of results: transport for primary PCI was superior to immediate thrombolysis in the first hospital, and the combination strategy (thrombolysis during transport) was intermediate (inferior to transport alone, superior to thrombolysis alone). Transportation decreased the incidence of the combined clinical end-point (death/reinfarction/stroke at 30 days). Thus, immediately after the PRAGUE-1 study we started preparing for a much larger nationwide trial, with 30-day mortality as the only primary end-point: the PRAGUE-2 trial. The aim was to compare intravenous streptokinase vs immediate transport for primary PCI in patients with ST elevation myocardial infarction, admitted to hospitals without PCI facilities in the Czech Republic, where distance between primary hospitals and tertiary PCI centres does not exceed 120 km.

Methods

The study protocol has been approved by the local ethical committees of all participating centres. The local ethical committee of the coordinating centre expressed concerns about the safety of long distance transport (i.e. not performing immediate thrombolysis) specifically in patients presenting within the initial 3 h after symptom onset. Thus, the committee required repeat interim reports about mortality to ensure that whenever a significant difference in favour of any group occurred the study would be stopped prematurely.

Infrastructure

The coordinating site was at the Cardiocenter, University Hospital Vinohrady, Prague, which was also one of the seven participating PCI centres. For at least 6 months before the start of the study in all seven PCI centres primary PCI was the only reperfusion strategy used in all patients presenting from their respective primary care region (these PCI centres had completely stopped using thrombolysis in their routine treatment of patients with acute myocardial infarction). Forty-one community hospitals without catheterization facilities were the primary sites. Patients were enrolled here into the study immediately after their initial ECG and after obtaining informed consent (Fig. 1).

Randomization and the treatment arms

Patients were randomized by telephone into one of the two arms (Table 1). The anti-thrombotic treatment prescribed by the protocol is also presented in Table 1 The attending physicians were allowed to change the strategy whenever they considered this to be of help for the patient. Specifically, intravenous use of GP IIb/IIIa inhibitors (abciximab or eptifibatide) was allowed in the PCI group and discouraged in the TL group (during the initial 24 h after streptokinase). No patient received GP IIb/IIIa blockers before the intervention. In four patients (1%) randomized to the PCI group the transport was cancelled due to rapid haemodynamic deterioration into profound cardiogenic shock soon after randomization. The four patients received thrombolysis, but they are analysed as the part of the PCI group, based on the intention-to-treat principle. For precise information a second (post-hoc) analysis was performed with respect to the final treatment (whether patients indeed received PCI or TL).

Patients

During the study period (23 September 1999–7 January 2002) a total of 4853 patients with any acute myocardial infarction presented to the emergency departments of 41 participating community

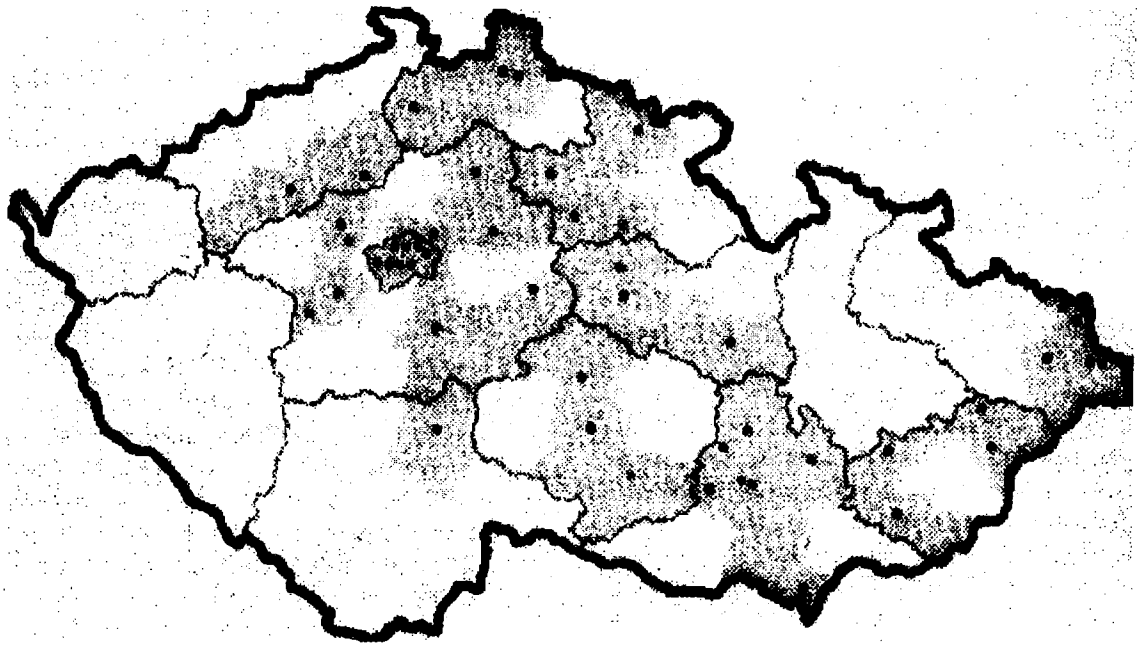


Figure 1 The map of the Czech Republic showing the geographic distribution of primary (community) hospitals/ tertiary cardiac centres (black points) along with their respective service areas-districts (grey). Thirty-three out of 77 districts (geographically 43% of the Czech districts) were participating in the study. The population of these districts however represents 5.7 million, i.e. 54% of the total country population. The situation in the country improved substantially during the study period. Thus, in 2002 additional 9 PCI centres were either newly opened or started 24-h service for primary PCI in acute myocardial infarction. Thus, at the end of study period, 95% of the Czech population had access to primary PCI at a distance <100 km from their homes.

Table 1 Treatment arms (reperfusion strategies)

Group TL (thrombolysis in the first hospital)	Group PCI (transportation to the tertiary PCI centre for primary PCI)
Patient stays in the primary hospital (transport allowed for rescue PCI or for recurrent ischaemia)	Transport to PCI centre immediately after randomization
Aspirin (Aspegic®) 500 mg iv.	Aspirin (Aspegic®) 500 mg iv.
	Heparin 200 U/kg iv.
Streptokinase 1.5 mil. U iv/45 min	PCI
Clopidogrel 75 mg for 1 month	Clopidogrel 75 mg for 1 month
Fraxiparin 0.8 ml sc. for 3 days	Fraxiparin 0.8 ml sc. for 3 days

hospitals without a catheterization laboratory. Eight hundred and fifty of them (who fulfilled the entry/exclusion criteria) have been randomized into one of the two treatment arms (Table 2). The remaining 4003 patients, who were not randomized, represent a mixture of non-ST elevation infarctions, late presenting Q-wave infarctions, contraindication for thrombolysis, refusal to sign informed consent and thrombolytic therapy or transport for primary PCI without randomization from various reasons. The only possible bias was that some physicians occasionally decided not to randomize some patients with anterior infarction and tended to send them for primary PCI without randomization. This is reflected by the some-what lower rate of anterior infarcts (40%). Another 2985 patients with ST elevation myocardial infarction presented during the same period directly (primary admissions) to the seven participating PCI centres. They were not randomized and have been treated routinely with immediate primary PCI and are not part of this study. (Information about the routine workload and results of the PCI centres are briefly described in Table 3 .) The inclusion criteria for the PRAGUE-2 study were: acute myocardial infarction (ST elevations > 1 mm in at least two leads or a new bundle branch block on initial ECG), within <12 h from the onset of symptoms, distance to PCI centre <120 km, feasibility to begin transport within 30 min after randomization, signed written

Table 2 Patients baseline characteristics

	TL group	PCI group
Number of randomized patients	421	429
Males (%)	71	70
Mean age (years)	64	65
Anterior infarction (%)	39	41
Previous infarction (%)	11	14
Diabetes mellitus (%)	23	25
Hypertension (%)	47	49
Previous CABG (%)	1.7	0.5
Previous PCI (%)	0.2	0.9
Heart Failure (Killip II–III) at the time of randomization (%)	16	16
Cardiogenic shock (Killip IV) at the time of randomization (%)*	1	2

TL = thrombolysis; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft. All differences in the characteristics between groups are not significant.

*After randomization (at any time during the hospital stay) cardiogenic shock developed in 11% of the TL group and 9% of the PCI group.

Table 3 Routine primary PCI results in the participating PCI centres during the study period (primary admissions, non-transported patients, are not part of the study population)

1 October 1999–7 January 2002	Primary/rescue PCI for AMI (n=)	Morphologic success rate-TIMI 2–3 (%)	In-hospital mortality (%)
Centre no. 1	621	91	8.2
Centre no. 2	331	87	7.3
Centre no. 3	387	94	4.6
Centre no. 4	718	96	5.6
Centre no. 5	163	na	4.9
Centre no. 6	532	97	2.8
Centre no. 7	287	91	9.1
Total	2985	93%	5.9%

informed consent. Exclusion criteria were: contraindication to thrombolysis (ischaemic stroke within previous 12 months, haemorrhagic stroke at any time, intracranial tumour, active internal bleeding, aortic dissection) and absence of bilateral femoral artery pulsations.

Coronary interventional procedure

Coronary angiography was performed via the femoral artery. The procedure was started by visualization of the 'non-infarct-related' coronary artery with a diagnostic 5–6F catheter and immediately thereafter the guiding catheter 6F was used for diagnostic visualization of the 'infarct-related' artery and for subsequent PCI. According to the protocol, PCI should be performed in all patients with TIMI flow 0–2 in the 'infarct-related' artery. When TIMI flow 3 was revealed on the acute coronary angiogram, it was left to the decision of the operator whether an intervention was to be performed in the acute phase, or later or not performed at all. A stent was implanted whenever anatomically suitable (vessel ≥3.0 mm in diameter, no extreme tortuosity), or when there was a suboptimal result (as assessed by the operator) after balloon angioplasty. Non-infarct-related arteries were not treated during the same procedure. Rescue PCI was defined as a percutaneous coronary intervention performed for continuing clinical and electrocardiographic signs of ischaemia after completion of the streptokinase infusion. The recommended policy was to decide within 30 min of the end of the streptokinase infusion whether to perform rescue PCI if ST elevations and chest pain continued.

Examinations and follow-up

Complete clinical examination with ECG was performed on days 1, 2, 3, at discharge and on day 30. Echocardiography was performed at discharge and

Table 4 The time delays to treatment (min)

	TL group	PCI group
Pain onset–randomization	173±119	183±162
Randomization–start of thrombolysis	12±10	na
Randomization–start of transport	na	20±9
Transport duration	na	48±20
Door–balloon time in the PCI centre	na	26±11
Randomization–reperfusion	na (cca 60–90')	97±28

on day 30. Coronary angiography was performed in the PCI group immediately on arrival at the PCI centre. In the TL group (as well as any repeat angiography in the PCI group) it was performed according to routine clinical indication: postinfarction angina pectoris, reinfarction, rescue PTCA after failed thrombolysis. Further 1-year follow-up is under way, but is not the subject of this paper.

Study end-points and definition

The primary end-point was mortality at 30 days. It was defined as death from any cause within 30 days after randomization. The secondary end-point was the presence of any serious clinical event (death/non-fatal reinfarction/non-fatal stroke) at 30 days. Furthermore, according to the suggestion of the ethical committee (see above), the 30-day mortality among subgroups of patients treated within 0–3 h and 3–12 h after symptom onset was added as a secondary end-point.

Stroke was defined as any new neurologic deficit lasting >24 h. Reinfarction was defined as recurrent symptoms of ischemia with new electrocardiographic changes and a rise in CK-MB. Optimal procedural success was defined as TIMI-3 flow and <30% stenosis after the intervention. Partial success (suboptimal result) was defined as TIMI-2 flow and/or >30% residual stenosis.

Statistic assessment

The calculated sample size was based on the expected mortality rates, similar to those in the PRAGUE-1 study. The target sample size was thus planned for 1200 patients. Microsoft Excel and Systat software were used for the database and chi-square was used for the statistical analyses of the differences between the two groups.

Results

Study termination

The study was stopped prematurely by the ethical committee. The reason was 2.5-fold excess mortality in the TL group among patients treated after >3 h from symptom onset. The committee considered thrombolytic treatment without transportation to the PCI centre no longer justified in this subset of patients (i.e. those treated between 3–12 h after symptom onset). There was also an increasing reluctance in the primary community hospitals to randomize the patients into the thrombolytic arm. These hospitals were increasingly asking for routine transportation of all patients with ST elevations during the study period.

Complications during transport

Four hundred and twenty-five patients (99%) in the PCI group were transported immediately after randomization to the PCI centre. The remaining four patients (1%) were not transported due to rapid haemodynamic deterioration into profound cardiogenic shock soon after randomization. All four patients were resuscitated and received thrombolysis, three of them died within the initial 24 h. They are analysed within the PCI group, based on the intention-to-treat principle. The distances between primary hospitals and PCI centres varied between 5–120 km. There were two deaths and three ventricular fibrillations (successfully treated with defibrillation in the emergency ambulance car, their further course was uneventful) during the transport (i.e. complications during the transport occurred in 1.2%).

The time delays and hospital stay

The treatment delays and transport time intervals are listed in Table 4 and Fig. 2 . The mean hospital stay duration in the TL group was 13±5 days and in the PCI group 11±4 days ($P<0.05$).

Coronary angiographic findings and PCI results

The infarct-related artery was left anterior descending in 158 patients, left circumflex in 55 patients, right coronary artery in 188 patients, left

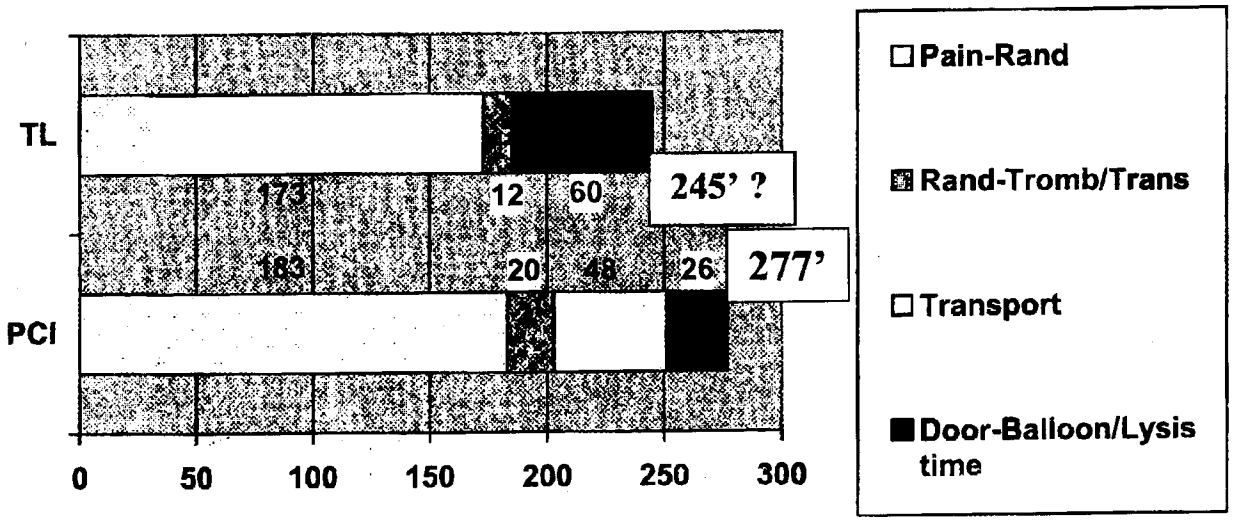


Figure 2 Time delays from the onset of symptoms to (presumed in TL) reperfusion. Patients were randomized after 173 and 183 min of symptoms respectively. The delay between randomization and thrombolysis start was 12 min and between randomization and transport start 20 min. Transport duration was 48 min. Door-to-balloon time was 26 min. To compare approximate reperfusion times, the presumed needle-reperfusion time of 60 min was added to the thrombolysis group. Thus the known total ischemia time in the PCI group was 277 min and the approximate ischaemic-reperfusion time in the thrombolysis group was 245 min.

main coronary artery in five patients and venous bypass graft in one patient. No angiography was performed in seven PCI group patients (four who finally were not transported, two who died during transport and one who received thrombolysis at the PCI centre due to technical problems in the catheter laboratory). The infarct-related artery was not defined in three patients. No significant coronary stenosis was found in 12 patients. TIMI-3 flow on the initial angiogram (pre-PCI) and immediately after PCI is shown in Fig. 3 . PCI was performed in 89% of all patients randomized to the PCI group. The full technical success rate of the interventions was 88%. There was a suboptimal result (TIMI-2 flow and/or residual diameter stenosis >30%) in 6% and the intervention was not successful in another 6% (TIMI flow 0–1 after PCI). Stents were implanted in 63% of all acute interventions. PCI success rates varied among the seven PCI centres between 85–90% (optimal success, TIMI 3 flow), and 92–100% (optimal + suboptimal success, TIMI 2–3 flow). In-hospital mortality among PCI centres varied between 2.6–9.4%. PCI was not performed in 49 PCI group patients (11%) for the following reasons: TIMI-3 flow and no pain at the time of angiography (20 patients), no significant stenosis at coronary angiography (12 patients), thrombolysis applied in the primary hospital (five patients), emergent coronary bypass surgery (three patients), chronic total coronary occlusion (two patients), death before PCI (two patients), miscellaneous (seven patients). Rescue PCI was performed in 27 TL group patients (i.e. 6.4% of streptokinase-treated patients).

Primary end-point

The 30-day mortality was 10.0% in the TL group (42 of 421 patients) vs 6.8% (29 of 429 patients) in the PCI group ($P = 0.12$).

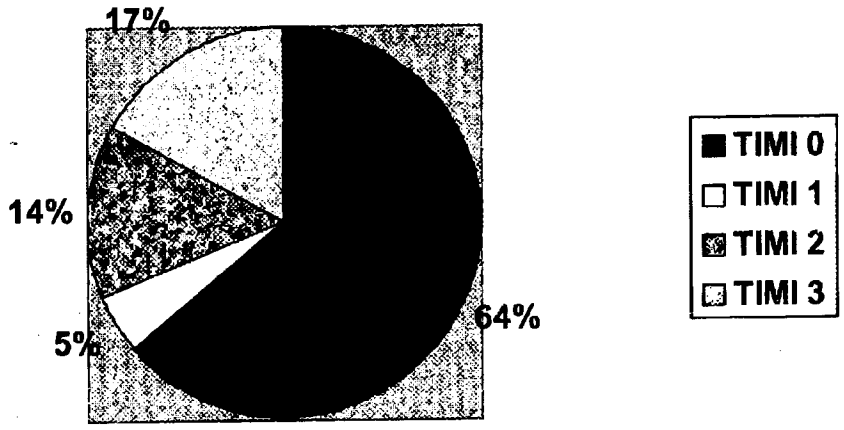
Secondary end-points

Among 299 patients randomized after >3 h (mean 5 h and 6 min) from symptom onset, the mortality was 15.3% in the TL group vs 6.0% in the PCI group ($P<0.02$). Among 551 patients randomized within <3 h (mean 1 h and 41 min) of symptom onset, the mortality was similar in both groups (7.4% in the TL group vs 7.3% in the PCI group) (Fig. 4). The combined clinical end-point (death/reinfarction/stroke) occurred in 64 TL group patients (=15.2%) vs 36 PCI group patients (=8.4%, $P<0.003$). There were 13 (=3.1%) non-fatal reinfarctions in the TL group vs six (=1.4%) in the PCI group (ns). Non-fatal stroke occurred in nine (=2.1%) TL patients vs one (=0.2%) PCI patient ($P<0.03$).

Analysis based on the actually used treatment

Primary PCI was performed in 380 patients (89%) of the PCI group. Their 30-day mortality was 6.0%.

Pre-PCI:



Post PCI:

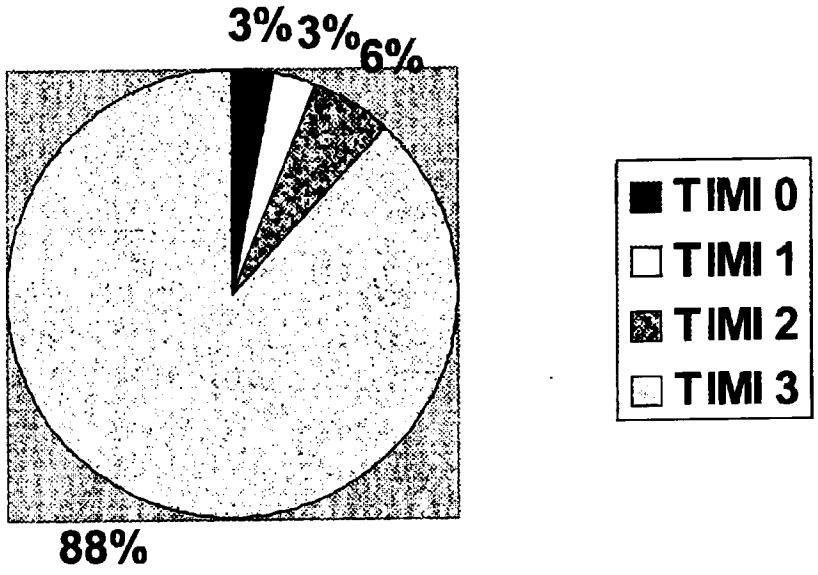


Figure 3 TIMI-flow before and after PCI.

Thrombolysis was used in 419 TL group patients and also in five PCI group patients (instead of PCI). The 30-day mortality of thrombolysed patients was 10.4% ($P<0.05$).

Left ventricular function

The mean echocardiographic left ventricular ejection fraction at 30 days was 51±9% in the TL group vs 50±8% in the PCI group (ns).

Discussion

Thirty-day mortality in the PCI group was almost exactly as expected based on the PRAGUE-1 study results (7%). However, mortality in the TL group was lower than expected 13%. Thus, the overall difference did not reach statistical significance. Nevertheless, the trend in favour of PCI strategy is clear. These data show a trend similar to that of DANAMI-2,[30] where the mortality difference was

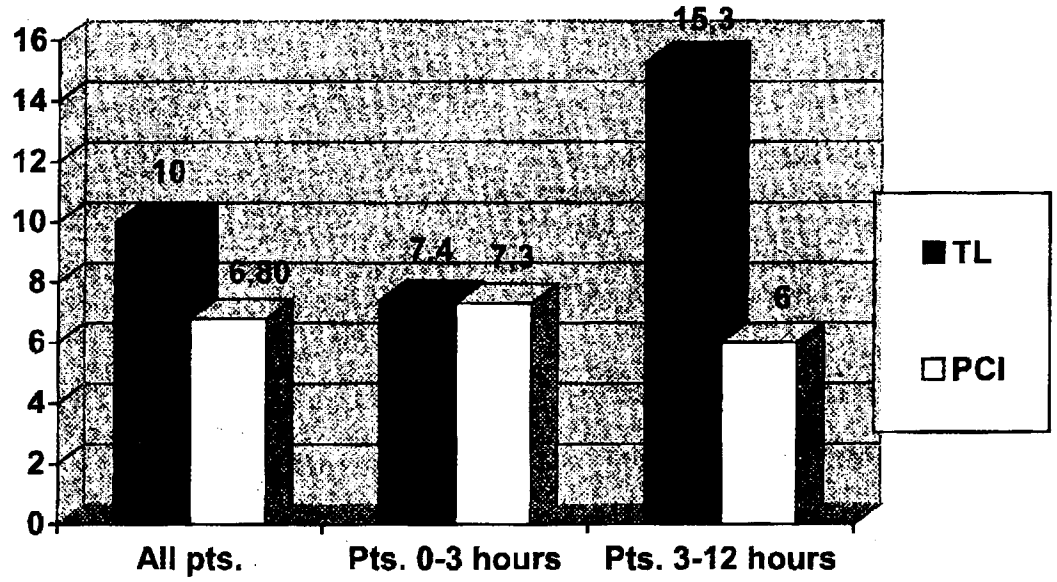


Figure 4 Thirty-day mortality (%) among all patients and among early vs late 'presenters'.

smaller, possibly due to use of t-PA instead of streptokinase.

The first 3 h of myocardial infarction

The results showed no harm from transport-related delays in the subgroup of 'early presenters' but did show a 2.5-fold increase in mortality among late presenters treated by thrombolysis. This is similar to the PCAT meta-analysis.[17] These studies support the strategy of primary PCI for every patient for whom PCI is available with only a short delay, compared to thrombolysis (i.e. short transport distances or primary admissions to PCI centres) and for every patient (even with a need for long transport distance) presenting after >3 h from symptom onset. Thrombolysis should be reserved only for those patients presenting within <3 h from symptom onset, with long, timely access to primary PCI. The study results do not show a difference between thrombolysis and PCI among patients with a presentation time <3 h, but this is not a statistical proof of equivalence; it would require a much larger study.

Patients presenting between 3–12 h after the onset of symptoms

The high mortality among TL group patients presenting after >3 h confirms the previous experience,[14,27] that thrombolysis is much less effective in these late presenters, while the effectivity of primary PCI is equal to the early presenters. The German MITRA/MIR registries showed no significant difference in mortality rates between primary angioplasty and thrombolysis for prehospital delays of <3 h. However, when pre-hospital delay was >3 h, thrombolysis was independently associated with a higher mortality rate compared with primary angioplasty.[18] Thus, the results of these studies support the change in the strategy for the late presenters—routine transfer for primary PCI should be the first choice. This is in accordance with the recent meta-analysis PCAT.[17]

Safety of transport in the acute phase of myocardial infarction

Several non-randomized observational reports[19–22] and two mentioned randomized trials[15,16] confirmed the feasibility and safety of transporting patients with acute myocardial infarction to tertiary centres for primary (or rescue) coronary angioplasty. There is a little doubt now, that the interhospital transport of patients with ST elevation acute myocardial infarction does not present any additional risk for the patient. What is the maximal distance for transport, for which the benefit of primary PCI will be offset by such an extensive time delay, that on-site thrombolysis will remain the preferable strategy? The published data are controversial in this respect. There is enough evidence that ischaemic time is related to infarct size and clinical outcome.[23–26] However, while delayed thrombolysis offers only very limited potential benefit to the patient,[28] primary PCI performed later (i.e. between 3–12 h from the onset of

symptoms) has a similar success rate and similar clinical outcome as in patients presenting within <3 h.[27–29]

Role of centre/operator experience

The variation among seven PCI centres was 87–97% for success rate and 2.8%–9.1% for in-hospital mortality among non-study patients. This reflects mainly the differences in routine decision making: the centres with lower mortality tended to exclude some really terminally ill cardiogenic shock patients or some elderly patients, while the centres with higher mortality rates do perform primary PCI in every patient without any age or terminal phase limits. However, the variation was relatively small and the results of all seven centres were similar among the study patients (where these differences could not have any influence, because the patients were randomized in other hospital). This is different from our previous experience[16] and reflects the increasing workload of the PCI centres in the Czech Republic during the last 5 years, when primary PCI became more frequent than thrombolysis as reperfusion therapy in the entire country.

Pharmacologic treatment before/after primary PCI

Another limitation of this study is that the thrombolytic arm was represented by streptokinase rather than more potent thrombolytic agents. Streptokinase was used because it is the routine treatment of myocardial infarction in the Czech Republic. However, the use of a more potent thrombolytic would probably not substantially affect the main results of the study (the difference between tPA and streptokinase could be hardly expected in a population of 421 patients in the TL group). In the recently presented DANAMI-2 trial tPA was used and the study was also terminated prematurely due to the convincing clinical benefit in the PCI group.[30]

Implications for the current practice

The data favouring primary PCI as the best available reperfusion strategy for patients with acute myocardial infarction are sound. The change in clinical practice should be considered in three directions: (1) Patients with ST elevations in areas with PCI availability within 20–30 min of transport time should always be transported directly from the emergency car/helicopter to the catheterization laboratory (avoiding delays in the small hospitals or emergency departments of the large hospitals). (2) When PCI cannot be started within 60 min of the ECG diagnosis, thrombolysis should be used—but only for patients presenting within <3 h of symptom onset. The usefulness of immediate angiography/intervention routinely after thrombolysis in these patients remains to be established. And finally (3) all patients presenting between 3–12 h from symptom onset should be transported for primary PCI and thrombolysis should not be used in this subset of patients. The data from this study together with data from other randomized trials and myocardial infarction registries should be brought together and a modification of guidelines may be considered.

Acknowledgements

The authors express thanks to the physicians, nurses and technicians of participating catheterization laboratories, coronary care units, community hospitals and regional emergency medical services.

Appendix

The complete list of investigators

PCI centres (number of patients randomized to the PCI group in the respective cooperating primary community hospitals): Investigators

Cardiocenter, University Hospital Vinohrady, Prague (110 patients): Petr Widimský, MD., DrSc., FESC., (principal investigator of the study). Tomáš Buděšínský, MD., *David Voráč, MD. (Junior research coordinator of the study),* Jaroslav Dvořák, MD., Jiří Krupička, MD., Libor Lisa, MD, Radovan Jirmář, MD., Pavel Gregor, MD., DrSc., FESC., Rudolf Špaček, MD., PhD, Zbynek Straka, MD, PhD.

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Cardiocenter, Hospital Podlesí, Třinec (72 patients): Marian Branny, MD., Igor Nykl, MD., Ivo Varvařovský, MD., Jindřich Černý, MD., Marek Richter, MD.

Cardiology Clinic IKEM, Prague (45 patients): Michal Želízko, MD., PhD., Bronislav Janek, MD., PhD., Jiří Kettner, MD., PhD., Vladimír Karmazín, MD.

Cardiocenter, University Hospital Hradec Králové (35 patients): Josef Šťásek, MD., Pavel Červinka, MD., Dušan Černohorský, MD., Miroslav Brtko, MD., Vladimír Rozsíval MD., PhD., Aleš Herman, MD., PhD.

Cardiology Department, Hospital Na Homolce, Prague (15 patients): Pavel Formánek, MD., Petr Kmoníček, MD., Ondřej Aschermann, MD.

Medical Department II, General University Hospital, Prague (5 patients): Michal Aschermann, MD., DrSc., Stanislav Šimek, MD., Aleš Linhart, MD., PhD., František Holm, MD., Jan Bělohlávek, MD.

Community hospitals (with total randomized patients) and investigators (all are MD)

Třebíč (62 patients): Josef Štumar, Jiří Carda, Ondřej Toman, Pavel Růžička, Petr Konečný. *Vyškov (59 patients):* Josef Veselý, Oldřich Synek, František Adamec, Vladimír Foret, Jiří Pinka. *Nymburk (57 patients):* Arnošt Václavíček, David Vencour, Michal Hudcovic, Pavel Frič, Radka Sytarová, Hana Širová, Václav Hulinský. *Havířov (57 patients):* Miloslav Durčák, Eva Pederzoliová. *Ivančice (49 patients):* Petr Valeš, Miroslav Čech. *Kutná Hora (42 patients):* Venuše Šmejkalová, Alena Kadlečková, Dana Ryšavá. *Slaný (42 patients):* Gabriel Marcinek, Ondřej Čermák, Jan Mácha. *Mladá Boleslav (38 patients):* Jiří Kotouš, Tomáš Kubiček, Zbyněk Košek. *Valašské Meziříčí (37 patients):* Pavel Prodělal, Marie Líčeníková, Richard Wiesner. *Vsetín (34 patients):* Jaroslav Doubravský, Jiří Ludva, Petr Palacký, Radmila Boháčová. *Tišnov (29 patients):* Jaroslav Vykouřil, Jaroslav Svoboda. *Havlíčkův Brod (24 patients):* Josef Málek, JiříŠtefánek. *Kroměříž (24 patients):* Lumír Francek, Pavel Třeštík. *Chrudim (23 patients):* Josef Tuhý, Dalibor Kašík, Michal Wysocki. *Vysočany (22 patients):* Eva Kosová, Jan Kaufman. *Uherské Hradiště (21 patients):* Vladimír Okénka, Vladimír Klapal. *Svitavy (20 patients):* Ivana Kellnerová, Emilie Smrčková. *Benešov (19 patients):* Václav Havlík, Martin Otava. *Hořovice (17 patients):* Eduard Kroupa. *Pardubice (16 patients):* Marek Sychra. *Roudnice nad Labem (14 patients):* Ilona Kašíková. *Břeclav (14 patients):* Jitka Siegelová. *Boskovice (14 patients):* Marie Lýčková. *Frýdek–Místek (14 patients):* Tomáš Gistinger. *Brandýs nad Labem (13 patients):* Richard Kobza. *Tábor (12 patients):* Jindřich Charouzek. *Louny (9 patients):* Jan Semrád. *Jičín (nine patients):* Soňa Zajíčková. *Liberec (7 patients):* Jiří Kot'átko. *Beroun (7 patients):* Karel Sochor. *Karviná (6 patients):* Jan Bolek. *Nový Bydžov (6 patients):* Luděk Beran. *Jihlava (6 patients):* Zdeněk Klimsa. *Na Františku (6 patients):* Ivo Jokl. *Turnov (5 patients):* Oldřich Honců. *Military Hospital Brno (5 patients):* Tomáš Brabec. *Military Hospital Prague–Střešovice (5 patients):* David Ručka. *Česká Lípa (3 patients):* Zdeněk Holý. *Na Žižkové (1 patient):* Zdeněk Felix. *Kladno (1 patient):* Jiří Povolný. *Třinec–Sosna (1 patient):* Jan Boháč.

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