

Impact of the time to reperfusion on early outcomes in patients with acute myocardial infarction undergoing primary angioplasty

Ewa Trzos, Małgorzata Kurpesa, Zbigniew Bednarkiewicz, Jan Peruga, Jarosław Kasprzak, Michał Plewka, Barbara Uznańska, Maria Krzemińska-Pakuła

Second Chair and Department of Cardiology, Medical University, Łódź, Poland

Abstract

Background: The ACC/AHA guidelines for management of patients with ST-elevation myocardial infarction (STEMI) have recommended primary PCI (pPCI) as the preferred reperfusion therapy, when it can be performed in a timely fashion, within 90-110 min from the first contact with medical personnel. The impact of treatment delays on outcomes in patients undergoing pPCI has been controversial.

Aim: To evaluate the impact of time delays on in-hospital mortality and on the frequency of cardiac events during 30 days after STEMI.

Methods: 1723 patients were stratified on the basis of their time delays: from symptom onset until balloon inflation. The patients were divided into 4 groups: group 1 (311 patients) – time from symptom onset <90 min; group 2 (731 patients) – time delays of 90-180 min; group 3 (535 patients) – time delays of 180-360 min, and group 4 (146 patients) – time from symptom onset >360 min.

Results: The median time delay was 268.5±206 min, the median door to balloon time was 36.12±11.2 min. The patients with longer time delays (group 4) were older, more often were women, and had a higher frequency of diabetes, anterior MI and Killip class 4. During hospitalisation, 70 (4.1%) patients died. In-hospital mortality was significantly higher in group 4 (13.6%) than in other groups. Complications of STEMI such as cardiogenic shock considerably influenced mortality (45.6%). During a 30-day follow-up, the patients with cardiogenic shock and the elderly had an increased risk of cardiac events. Also, time delays >360 min and failed pPTCA were independent adverse risk factors in multivariate regression analysis.

Conclusion: Delays in time to pPCI have an impact on outcomes, especially in those treated >6 hours from the onset of symptoms.

Key words: myocardial infarction, primary angioplasty, prognosis

Kardiologia Polska 2007; 65: 1296–1304

Introduction

Findings of many studies indicate that primary percutaneous coronary intervention (pPCI) in patients with ST-segment elevation myocardial infarction (STEMI) significantly reduces mortality, incidence of recurrent MI, number of hospital readmissions shortens, the rate of haemorrhagic complications and in-hospital stay [1, 2]. It has been shown that pre- and in-hospital delay may result in unfavourable outcome of treatment with pPCI. The following scheme of pathological changes within myocardium during ischaemia signifies deleterious effects of delay in the initiation of reperfusion: ischaemia <20 min – cardiomyocyte oedema (early changes are

likely to reverse completely); ischaemia >60 min – progressive cardiomyocyte oedema; approximately 90 min of ischaemia – irreversible necrosis of 40-50% of cardiomyocytes confined to the infarcted area; >6 hours – coagulative oedema involving virtually 100% of cardiomyocytes unless collateral circulation is well developed.

The aim of this study was:

- 1) analysis of early results of ST-segment elevation acute coronary syndrome (STE-ACS) treatment with the use of pPCI in relation to in-hospital delay time;
- 2) identification of the most significant clinical variables affecting an early, 30-day prognosis.

Address for correspondence:

Ewa Trzos MD, II Katedra i Klinika Kardiologii, Wojewódzki Szpital Specjalistyczny, ul. Kniaziewiczza 1/5, 91-347 Łódź, tel.: +48 42 251 60 34, e-mail: ewa_trzos@op.pl

Received: 18 February 2007. **Accepted:** 08 August 2007.

Methods

Patients

The examined group involved 1802 patients with acute MI hospitalised in the Second Cardiology Chair and Department of Łódź Medical University from 2001/01/06 to 2004/31/05 and treated within the framework of the interventional programme of STE-ACS management, transported directly or transferred from other hospitals to our centre with cath-lab on stand-by availability. At the time of hospital admission, all patients fulfilled criteria for acute MI diagnosis such as 1) duration of chest pain from 30 min to 12 hours (excluding patients found to be in cardiogenic shock); 2) presence of ST-segment elevation of more than 1 mm in at least two limb leads and/or by ≥ 2 mm in at least 2 precordial leads, or new or presumably new left bundle branch block (LBBB).

Complete clinical examination was performed in all patients prior to qualification for invasive therapy. Additionally, blood samples were taken to measure levels of markers (CK, CK-MB and Troponin I) as well as glucose, creatinine and electrolytes concentrations. After informed patient consent for invasive procedure was obtained, coronary angiography followed by angioplasty of the infarct-related artery (IRA) was carried out. The decision to implant a stent was operator-dependent. The PCI procedure was considered successful if TIMI 3 grade flow was achieved with residual stenosis $\leq 30\%$. Patients after failed fibrinolysis followed by rescue angioplasty and those selected for coronary artery bypass grafting based on coronary angiography findings were excluded from this analysis.

The 1723 fulfilled the above-mentioned criteria and patients were divided into 4 groups according to the reperfusion delay times (i.e. the time period from the onset of chest pain to first balloon inflation during pPCI); group 1 involved 311 patients with delay time not exceeding 90 min; group 2 comprised 731 patients with delay time ranging from 90 to 180 min; group 3 comprised 535 patients with time delay between 180 and 360 min, and group 4 comprised 146 patients with the longest delay time, exceeding 360 min.

Analysed parameters

Complete clinical evaluation and additional examinations were performed in each patient. Clinical evaluation included analysis of the following variables:

- 1) infarct area estimated based on ECG, biochemical and echocardiographic findings (left ventricular ejection fraction),
- 2) clinical and ECG signs of reperfusion,
- 3) results of angiography, efficacy of flow restoration in IRA according to the TIMI classification,
- 4) incidence of repeat MI, stroke or repeat urgent revascularisation,
- 5) haemorrhagic complications,
- 6) duration of hospitalisation,
- 7) in-hospital mortality.

Follow-up

All patients after discharge were subjected to follow-up. Most of them were referred to stage II of in-hospital or out-patient cardiac postinfarction rehabilitation programme. All patients had an appointed follow-up examination in the Cardiac Outpatient Clinic within 4 to 8 weeks after MI. Information regarding clinical status of some patients was collected by direct contact with the hospital departments, where they transferred in order to complete the therapeutic process. This group involved patients who required prolonged mechanical ventilation in specialised intensive care centres. During a 30-day follow-up cardiovascular mortality, rate of repeat MI, stroke and the need for repeat coronary revascularisation were assessed. The primary composite end-points included death, repeat MI or stroke.

Statistical analysis

Continuous variables are presented as mean \pm standard deviation. The χ^2 test was used to compare the incidence of discrete variables in the examined groups of patients. Continuous variables were compared by means of univariate analysis of variance with multiple comparison test. An univariate logistic regression analysis was used to evaluate the impact of the selected variables on the composite primary end point. A multivariate logistic regression was adopted for detection of the group of factors with the most pronounced impact on risk of adverse cardiac events. A p value < 0.05 was considered significant. The statistical software package Statistica PL version 5.5 was used for all calculations.

Results

According to the protocol of the management of MI patients adopted in our region, patients diagnosed by an ambulance physician were referred directly to our centre. A total of 1175 (68.2%) patients were transported directly from their homes by ambulance while 548 (31.8%) of study participants were transferred from other hospitals within either the city borders or the region. A group of patients transported from outside the city of Łódź comprised 916 individuals and the mean transport time was 54.5 ± 17.8 min.

Baseline patients' characteristics

Demographic and clinical data on the risk factors and previous cardiovascular events such as MI, stroke and myocardial revascularisation are presented in Table I. There were significant demographic differences between the examined groups. Patients of group 4 with the longest delay time were significantly older than those from groups 1 or 2 and had significantly higher representation of females. Moreover, in group 4 the highest prevalence of diabetes mellitus was noted. The prevalence of other risk factors such as smoking, arterial hypertension, dyslipidaemia and previous cardiovascular events did not differ between the groups.

Selected baseline clinical parameters are presented in Table II. One hundred fourteen patients were found to be in cardiogenic shock. The percentage of patients admitted to hospital with cardiogenic shock was significantly higher in group 4, as was the number of individuals surviving cardiac arrest. Group 4 patients had significantly higher heart rate and higher prevalence of anterior MI as well as atrial fibrillation (AF).

Angiographic characteristics and pPCI results are shown in Table III. Most commonly, an occlusion of the right coronary artery was diagnosed. Lesions' localisation and their extension differed between the groups. The

occlusion of the left anterior descending coronary artery and left main stem disease were significantly more frequent in group 4, in which the percentage of subjects with multi-vessel disease was also higher.

The pPCI procedure was successful in 1649 (95.7%) patients and in 85.5% of them TIMI 3 grade flow was restored with residual stenosis of <30% (see Table III). The highest rate of patency restoration was achieved in group 1. Stents or stent-grafts were implanted in 1168 (67.8%) patients. Glycoprotein IIb/IIIa inhibitors were administered in 75.3% of patients. The percentage of early reocclusions of IRA was low (1.7%), while the rates of reocclusion and

Table I. Baseline demographic characteristics of the studied groups

Parameter	Group 1 (n=311)	Group 2 (n=731)	Group 3 (n=535)	Group 4 (n=146)	p	Overall (n=1723)
Age (mean±SD) [years]	52.3±15.2	55.5±19.3	58.7±15.7	67.2±17.2	<0.05**	60.5±21.2
Female gender	92 (29.5%)	271 (37.1%)	201 (37.6%)	82 (56.2%)	<0.05*	616
Hypertension [%]	30.4	35.2	40.2	47.5	NS	37
Dyslipidaemia [%]	35.3	31.2	38.7	43.2	NS	35.2
Smoking [%]	31.2	23.2	35.3	19.5	NS	27.9
Angina de novo [%]	13.4	15.9	19.5	10.2	NS	16
Previous myocardial infarction [%]	10.1	20.1	17.2	9.8	NS	16.4
History of stroke [%]	0	2.3	2.7	4.1	NS	2.14
Diabetes mellitus [%]	9.7	16.2	23.3	38.1	<0.05*	14.5
Previous myocardial revascularisation [%]	3.2	2.1	3.4	1.9	NS	2.7

* group 4 vs. group 1, 2 or 3; ** group 4 vs. group 1 and vs. group 2

Table II. Clinical characteristics of the studied groups. Data are expressed as percent of patients or mean values ± SD

Parameter	Group 1 (n=311)	Group 2 (n=731)	Group 3 (n=535)	Group 4 (n=146)	p	Overall (n=1723)
Killip class [%]						
I	62.8	60.7	46.5	13.0	<0.05**	52.9
II	33.4	27.5	36.5	48.1		32.7
III	1.9	7.1	9.1	20.5		7.8
IV	1.9	4.7	8.9	18.4		6.6
History of cardiac arrest prior to admission [%]	1.2	3.6	6.0	16.4	<0.05**	4.8
Unconscious; intubated [%]	0.64	0.55	1.3	6.9	<0.05**	1.3
Myocardial localisation in ECG [%]						
anterior wall	37	39.5	43	65.3	<0.05**	42.3
inferior wall	63	60.5	57	34.7		57.7
Pathological Q-wave [%]	0	19.2	32.3	40.8	<0.05*	21.5
Left bundle branch block [%]	2.3	4.3	5.8	8.3	NS	4.7
Atrial fibrillation [%]	0.4	1.2	3.6	15.2	<0.05**	2.9
Heart rate [beats/minute]	70±13.2	75±17.6	83±18.3	94±21.2	<0.05*	79.7±16.2
CK-MB on admission [U/l]	60.2±22.1	67.2±18.2	63.3±21.5	68.5±27.2	NS	61.3±19.3
Troponin I on admission [mg/ml]	2.12±1.75	2.02±2.11	4.37±2.85	5.6±4.3	NS	3.45±3.2
Baseline creatinine concentration [mg/ml]	1.08±0.44	1.12±0.52	1.16±0.77	1.23±0.83	NS	1.14±0.75

* group 4 vs. group 1 and 2, ** group 4 vs. group 1, 2 or 3

the need for repeat angiographic procedure were significantly higher in group 4.

In-hospital outcomes

The clinical course during hospitalisation is presented in Table IV. Mean in-hospital delay time, defined as the time period from admission to the hospital to the first balloon inflation, also called door-to-balloon time, was 36.12 min and was found to be the shortest in group 1, although differences between the groups did not reach statistical significance.

At 90 min following IRA flow restoration, ECG signs of reperfusion (depression of the previously elevated ST-segment by more than 50%) were observed in 85.2% of patients. The successful reperfusion rate was high in group 1 and in group 2 while in group 4 it was the lowest (64.5%). Left ventricular ejection fraction was usually

evaluated on the third day of hospitalisation. The lowest value was recorded in group 4, but the differences were significant only when compared with group 1.

Haemorrhagic complications were noted in 4.7% of the whole patient group and were diagnosed most often in group 4. Repeat MI rate was also the highest in group 4. Seventy patients died in hospital. The highest mortality (45.6%) was seen in a group of 114 patients admitted to hospital with cardiogenic shock. The highest group-adjusted mortality was found in group 4.

Up to day 30 of follow-up, 8 other patients died from cardiovascular reasons. Thus, overall mortality during 30-day follow-up was 4.5%. The incidence of other cardiovascular events is outlined in Table V. The highest mortality and rate of aforementioned cardiovascular adverse events were noted in group 4 – these differences were of statistical significance compared to the other three studied groups (Table V).

Table III. Angiographic data and the results of primary PCI in the studied groups. Data are expressed as percentages

Parameter	Group 1 (n=311)	Group 2 (n=731)	Group 3 (n=535)	Group 4 (n=146)	p	Overall (n=1723)
Infarct-related coronary artery						
left main coronary artery	0.6	0.8	1.8	6.2	<0.05*	1.5
left anterior descending artery	16.3	38	45.8	59	<0.05*	38.3
circumflex artery	29	11.5	16.5	10.5	NS	17.0
right coronary artery	54.1	49.7	35.9	24.5	NS	43.2
Severity of coronary artery disease						
one-vessel	54.8	45.2	21.6	10.3	<0.01*	36.5
two-vessel	31.8	35.6	43.2	29.5	NS	36.7
three-vessel	13.4	19.2	35.2	53.2	<0.05*	26.7
Final flow in the infarct-related artery (TIMI)						
3	98.3	86.6	80.5	73.4		85.5
1-2	1.7	10.1	12.8	16.8	<0.05**	10.2
0	0	3.3	6.7	9.8		4.3
Coronary reocclusion during hospitalisation	0	0.9	1.5	11.6	<0.05*	1.76
Repeated PCI	0	1.2	2.8	7.6	<0.05*	2.03

* group 4 vs. group 1, 2 or 3; ** group 1 vs. group 2, 3 or 4

Table IV. In-hospital course. If not indicated, data are presented as percent of patients

Parameter	Group 1 (n=311)	Group 2 (n=731)	Group 3 (n=535)	Group 4 (n=146)	p	Overall (n=1723)
In-hospital delay time (mean ± SD)	24.5±9.2	37.4±18.3	36.2±13.2	40.3±14.6	NS	36.12±11.2
Signs of reperfusion in ECG	93	90.5	80.5	64.5	<0.05**	85.2
Mean left ventricular ejection fraction [%]	48.2±13.4	43.3±15.6	40.4±10.2	31.4±11.3	0.05***	42.7±8.1
Haemorrhagic complications (overall)	1.2	4.3	4.6	9.2	<0.05*	4.7
Repeat myocardial infarction	0.3	1.1	1.3	7.5	<0.05*	1.5
Stroke	0	0.4	0.6	3.4	NS	0.64
In-hospital death	1.3	3.5	4.2	13.6	<0.05*	4.1

* group 4 vs. group 1, 2 or 3; ** group 1 or 2 vs. group 4; *** group 4 vs. group 1

Table V. Incidence of major cardiovascular events in the examined groups of patients during a 30-day follow-up. Data are expressed as percent of patients

Parameter	Group 1 (n=311)	Group 2 (n=731)	Group 3 (n=535)	Group 4 (n=146)	p	Overall (n=1723)
Cardiac death	1.9	3.7	4.6	14.3	<0.05*	4.5
Repeat myocardial infarction	0.3	1.2	1.4	8.2	<0.05*	1.6
Stroke	0	0.4	0.7	4.1	<0.05*	0.7
Repeat revascularisation	0	1.36	3.2	8.2	<0.05*	2.2

* group 4 vs. group 1, 2 or 3

Table VI. Impact of selected factors on the occurrence of composite end point within 30-day follow-up

Variable	95% CI	OR	p
Age >75 years	2.64-7.8	3.821	0.001
Onset of symptoms 0-2 hours			>0.1
Onset of symptoms 2-4 hours			>0.1
Onset of symptoms >6 hours	1.0-4.1	2.071	0.045
Diabetes mellitus			>0.1
Hypertension			>0.1
Gender			>0.1
Smoking			>0.1

Table VII. Impact of selected clinical, ECG and angiographic variables on the occurrence of composite primary end point during 30-day follow-up

Variable	95% CI	OR	p
Killip class >2	2.3-10.13	5.315	0.005
History of cardiac arrest	1.0-11.3	3.067	0.021
Heart rate >79/min	1.4-5.5	2.341	0.027
Left bundle branch block			>0.1
Atrial fibrillation	0.8-4.5	1.513	0.036
Signs of reperfusion on ECG			>0.1
Creatinine >1.14 mg/dl			>0.1
Left main trunk stenosis	1.2-8.7	3.429	0.028
PCI efficacy	0.11-0.92	0.331	0.043

Table VIII. A model of multivariate logistic regression with respect to the risk of composite primary end point occurrence during 30-day follow-up

Variable	95% CI	OR	p
Cardiogenic shock	2.1-14.5	8.323	0.001
PCI efficacy	0.08-0.82	0.21	0.035
Age >75 years	2.2-8.6	4.126	0.005
Delay time >6 hours	0.99-3.2	1.72	0.023

The relationship between selected factors and the risk of composite primary end point during 30-day follow-up was also analysed (Tables VI and VII). The following risk factors were found to be significant predictors in the univariate analysis: age >75 years, and time from the onset of pain exceeding 6 hours (Table VI). Among selected clinical data a significant relationship was noted for Killip class >2, cardiac arrest, heart rate >79 beats/minute, AF, left main trunk stenosis and pPCI efficacy according to the TIMI scale. Variables with significant predictive value assessed by univariate analysis were included in the model of multivariate logistic regression to identify independent predictors. The multivariate model for the assessment of 30-day risk predictors included 4 variables: age >75 years, delay time >6 hours, cardiogenic shock and PCI efficacy (Table VIII), whereas gender, concomitant diabetes mellitus, hypertension and smoking did not independently affect the risk of the composite end-point.

Discussion

The principal advantage of the invasive treatment of STE-ACS compared to fibrinolytic therapy is the higher rate of IRA flow restoration (85-90 vs. 65%) [3, 4]. The ACC/AHA and ESC Guidelines recommend reperfusion therapy in patients with STEMI within 12 hours from the onset of MI symptoms. Primary PCI is the method of choice in patients with contraindications to fibrinolysis and those in cardiogenic shock even if delay time exceeds 12 hours. Primary PCI is the recommended first choice in all STEMI patients if available within the first 90 min, or even 120 min from the first medical contact [5, 6]. It is known that prolonging delay time worsens the prognosis of STEMI patients treated with fibrinolysis [7-9]. Meanwhile, in the groups of patients treated with pPCI, the findings regarding correlations between delay time of reperfusion therapy and survival are not so clear [3, 4, 10]. Thus, the purpose of our study was to analyse the early results of STE-ACS treatment with pPCI in relation to the time period from symptoms onset to balloon inflation duration.

During in-hospital stay, the highest mortality rate was noted in the group of patients with the longest delay time of reperfusion therapy (>360 min). Overall mortality in the examined population was 4.1%. A similar mortality rate

(4.4%) was observed in the PL-ACS pilot registry of the Silesian region in years 2003-2004 [11].

Many authors have shown a relationship between time period to reperfusion with pPCI and risk of death during follow-up. In the analysis by Brodi et al. 30-day mortality was the lowest in a group of patients treated with pPCI within 2 hours from the onset of pain, being 4.3%. In the consecutive time periods (2-4 hours, 4-6 hours, >6 hours) a marked increase in mortality rate to as high as 9.5% was noted [12]. However, the authors of the National Registry of Myocardial Infarction (NRFMI 1-2 and NRFMI 3-4) did not find a significant correlation between time from symptoms onset to pPCI and mortality rate in the early follow-up after MI [10, 13, 14].

Some authors employ in their analyses so-called door-to-balloon time, i.e. time from hospital admission to pPCI procedure due to methodological problems with precise establishment of chest pain onset time [15, 16]. These analyses revealed significantly increased risk of death with increased time from hospital admission to balloon inflation [13, 16, 17]. Such a correlation was observed in the NRFMI population, and in the study of MacNamara et al. [16] this relationship was particularly strong and independent from the baseline risk profile. A different opinion was presented by De Luca et al., who did not confirm an impact of door-to-balloon time on the risk of death while showing that time from onset of pain to balloon inflation was an independent prognostic factor [18].

In our study, total delay time from symptoms onset to reperfusion therapy initiation was analysed, including transport time. Mean delay time was 268.5 ± 206 min for the whole examined population and its division into four groups was based on the duration of this delay. Average in-hospital delay time was 36.12 ± 11.2 min for the whole population. It did not differ between the groups. In the study reporting results of STEMI patients treatment in our centre in years 2001-2002, pre-hospital delay time was shorter (224 ± 102 min), but in-hospital time comparable (mean 32 min) [19]. In the Institute of Cardiology in Warsaw, in-hospital door-balloon delay time was reduced to a median of 43 min [20]. Similarly, in many Polish centres in-hospital delay time did not exceed 55 min and was markedly shorter when compared to data of the NRFMI registries, in which door-to-balloon delay exceeded 90 min in most cases [10, 13, 14].

It seems that the assessment of impact of delay on prognosis should not be limited just to door-to-balloon delay time analysis, but should involve total delay time of reperfusion, from the symptom onset to balloon inflation. Such evaluation may be of special importance considering data suggesting a delay from pain onset to reperfusion to be an independent risk factor of increased mortality rate, particularly in the high-risk patient groups [15, 18]. Pilot results of PL-ACS show that approximately 61% of patients are transferred to the catheterisation laboratory from their homes and in 66.7% of patients pre-hospital

delay time does not exceed 6 hours [11, 21]. However, the treatment of patients who reach centres of interventional cardiology after a prolonged time remains problematic.

In our study a small percentage (8.5%) of the examined population had a delay time of more than 360 min. Patients in this group were older, more frequently were females, and had increased prevalence of diabetes mellitus and anterior MI as well as symptoms of heart failure, including cardiogenic shock. Mortality was the highest in this group, amounting to 13.6%. One may ask if it resulted only from delay as patients of this group presented the highest number of factors with an adverse impact on prognosis. It seems that this is true, as the time factor remained an independent risk factor in both uni- and multivariate analysis. It was stressed in many previous reports that prolongation of time from the pain onset to reperfusion therapy initiation was usually seen in the elderly. In the GUSTO study, delay in a group of patients aged 65 years or older was higher by 40 min compared with younger individuals [22]. In the elderly, the prolonged delay may be related to the atypical clinical presentation as well as higher percentage of early complications requiring additional procedures such as temporary pacing.

In a group of 311 (18%) patients who underwent pPCI procedure within 90 min from the symptom onset, the highest rate of blood flow restoration (98.3%), lowest mortality (1.3%) and complication rate during in-hospital or 30-day follow-up were observed. A prompt call for ambulance, fast and direct patient transport to the cardiology centre and call for physicians on duty in the catheterisation laboratory as well as intensive cardiology care units have contributed to favourable outcomes in this group of patients. Such a management also enabled the reduction of door-to-balloon time to a mean of 24.5 min. Patients in this group were significantly younger, but of note 33.4% of them had heart failure symptoms defined as Killip class II and in 37% anterior MI was diagnosed.

In our study, age >75 years, delay time >6 hours, Killip class >2, sudden cardiac arrest, heart rate >79/minute, AF, pPCI efficacy according to TIMI scale and significant stenosis of left main stem were significantly associated with an adverse outcome. In the multivariate logistic model, however, four variables – cardiogenic shock, age, delay time and PTCA efficacy – remained significant with respect to the impact on composite primary end point.

In the majority of studies age was shown to be an independent prognostic factor in STEMI patients. For example, in the GUSTO trials patient age was found among 6 independent risk factors of mortality [22, 23]. These studies revealed a 100% increase in mortality for every 10 years increase of age. On the other hand, in many elderly patients pPCI may be a valuable treatment method due to frequent contraindications to thrombolysis, more severe clinical course of MI and common comorbidities [24].

Cardiogenic shock is a recognised, adverse predictive factor in patients with ACS. In our study it also proved

significant, increasing 8-fold the risk of composite end point within 30-day follow-up. In our study, 114 (6.6%) patients developed symptomatic cardiogenic shock and it was detected most often in the group with the longest reperfusion delay (in 18.4%). Mortality of patients found in cardiogenic shock was high (45.6%). Similar were results from the 2002 registry from Katowice [25]. However, in a pilot registry of PL-ACS regarding the results of treatment in the Silesian region between 2003 and 2004, the rate of both cardiogenic shock (12.1%) and its related mortality (52.4%) were higher [11]. Registry analyses with respect to patients with MI complicated by cardiogenic shock proved that achievement of TIMI 3 grade flow in IRA may increase survival even by 75% [26-28]. Thus, in this setting, the only chance is rescue PCI, which is justified even after a delay as long as 18 hours.

Pre- and in-hospital sudden cardiac arrest is associated with three-fold increased risk of adverse cardiac events later on. These complications were observed in 83 (4.8%) patients, most frequently in group 4 patients. Reports investigating the impact of sudden cardiac arrest on risk of complications in STEMI patients are scarce. Barbash et al. reported mortality of approximately 60% in a group of 220 patients who underwent rescue pPCI after sudden cardiac arrest [29].

Complete reperfusion is a factor with a significant impact on survival following MI. Patients with blood flow in IRA assessed as 0-2 according to the TIMI scale manifest worse prognosis: higher mortality, increased rate of heart failure or ischaemic events as compared to patients in whom complete flow restoration (TIMI 3) was achieved [30]. In our study normal coronary flow following PCI (TIMI 3) markedly decreased the risk of complications after MI. It should be stressed however that patency of IRA is not always associated with adequate tissue reperfusion. Thus, flow evaluation at the microcirculatory level enables further risk stratification of this factor in acute MI [31].

Another factor associated with two-fold increase of the risk of serious cardiovascular events is heart rate. In the early 1990s, the significant prognostic value of this simple clinical parameter in predicting outcomes following MI was documented [32, 33]. Currently, extensive interest in this predictive but seemingly forgotten factor is observed. In discussing the heart rate issue it is worth mentioning that in our study AF markedly increased the risk of complications. Similarly, in the other observations arrhythmia of that kind significantly worsened the prognosis [34]. One of the GRACE registry sub-analyses showed that the prognosis in patients with AF was worse than in patients free from AF [35]. However, in the multivariate analysis AF lost its prognostic significance, which is also confirmed by the findings in our study.

In summary, the results of our study confirmed a high pPCI efficacy in the STEMI treatment. In-hospital mortality was 4.1% and the rate of the composite end-point during

30-day follow-up was relatively low (cardiac death 4.5%, repeat MI 1.6%, and stroke 0.7%). It should be emphasised that our study included also patients who were excluded from many previously published trials, such as unconscious patients, patients with cardiogenic shock and the elderly. Our findings further support the efficacy of STEMI treatment with pPCI in a such unselected group of patients.

Conclusions

- 1) Primary PCI used for the treatment of STE-ACS is associated with low in-hospital (4.1%) and 30-day (4.5%) mortality.
- 2) The outcomes depend on the reperfusion delay time, being the worst in patients with delay exceeding 6 hours from the onset of pain.
- 3) Time from the onset of symptoms >6 hours, cardiogenic shock, failed pPCI, and age of more than 75 years were found to be independent predictors of adverse cardiovascular events in a 30-day follow-up.

References

1. Julian D, Braunwald E. Heart disease: A Textbook of Cardiovascular Medicine. General hospital management. In: Julian D, Braunwald E (ed.). Management of acute myocardial infarction. *WB Saunders*, London 1994; 31.
2. Keeley EC, Boura JA, Grines CL, et al. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003; 361: 13-20.
3. Grines CL, Westerhausen DR Jr, Grines LL, et al. A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the Air Primary Angioplasty in Myocardial Infarction study. *J Am Coll Cardiol* 2002; 39: 1713-9.
4. Zahn R, Schiele R, Schneider S, et al. Primary angioplasty versus intravenous thrombolysis in acute myocardial infarction: can we define subgroups of patients benefiting most from primary angioplasty? Results from the pooled data of the Maximal Individual Therapy in Acute Myocardial Infarction Registry and the Myocardial Infarction Registry. *J Am Coll Cardiol* 2001; 37: 1827-35.
5. Silber S, Albertsson P, Aviles FF, et al. Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. *Eur Heart J* 2005; 26: 804-47.
6. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004; 44: E1-E211.
7. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. *Lancet* 1994; 343: 311-22.
8. Newby LK, Rutsch WR, Califf RM, et al. Time from symptom onset to treatment and outcomes after thrombolytic therapy. GUSTO-1 Investigators. *J Am Coll Cardiol* 1996; 27: 1646-55.

9. Goldberg RJ, Mooradd M, Gurwitz JH, et al. Impact of time to treatment with tissue plasminogen activator on morbidity and mortality following acute myocardial infarction (The second National Registry of Myocardial Infarction). *Am J Cardiol* 1998; 82: 259-64.
10. Nallamothu BK, Bates ER, Herrin J, et al. NRM Investigators. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRM)-3/4 analysis. *Circulation* 2005; 111: 761-7.
11. Poloński L, Gąsior M, Gierlotka M, et al. Epidemiologia, leczenie i rokowanie w ostrych zespołach wieńcowych na Śląsku. Wyniki etapu pilotażowego ogólnopolskiego rejestru ostrych zespołów wieńcowych PL-ACS. *Kardiologia Polska* 2005; 62 (Supl. I): 122-127.
12. Brodie BR, Stone GW, Morice MC, et al. Importance of time to reperfusion on outcomes with primary coronary angioplasty for acute myocardial infarction (results from the Stent Primary Angioplasty in Myocardial Infarction Trial). *Am J Cardiol* 2001; 88: 1085-90.
13. Cannon CP, Gibson CM, Lambrew CT, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA* 2000; 283: 2941-7.
14. Shavelle DM, Rasouli ML, Frederick P, et al. Outcome in patients transferred for percutaneous coronary intervention (a national registry of myocardial infarction 2/3/4 analysis). *Am J Cardiol* 2005; 96: 1227-32.
15. Brodie BR, Hansen C, Stuckey TD, et al. Door-to-balloon time with primary percutaneous coronary intervention for acute myocardial infarction impacts late cardiac mortality in high-risk patients and patients presenting Early after the onset of symptoms. *J Am Coll Cardiol* 2006; 47: 289-95.
16. McNamara RL, Wang Y, Herrin J, et al. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction. *J Am Coll Cardiol* 2006; 47: 2180-6.
17. Berger PB, Ellis SG, Holmes DR Jr, et al. Relationship between delay in performing direct coronary angioplasty and early clinical outcome in patients with acute myocardial infarction: results from the global use of strategies to open occluded arteries in Acute Coronary Syndromes (GUSTO-IIb) trial. *Circulation* 1999; 100: 14-20.
18. De Luca G, Suryapranata H, Zijlstra F, et al. ZWOLLE Myocardial Infarction Study Group. Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. *J Am Coll Cardiol* 2003; 42: 991-7.
19. Kasprzak JD, Peruga JZ, Foryś J, et al. Wyniki leczenia zawału serca metodą pierwotnej koronaroplastyki w roku 2002. Raport z Kliniki Kardiologii IMW UM w Łodzi. *Kardiologia Polska* 2003; 58 (Supl. IV): 44.
20. Karcz M, Kępka C, Bekta P, et al. Wyniki zabiegowego leczenia pacjentów z ostrym zawałem serca lub ostrym zespołem wieńcowym bez uniesienia odcinka ST – podsumowanie pierwszego roku całodobowego dyżuru kardiologii interwencyjnej w Instytucie Kardiologii w Warszawie-Aninie. *Kardiologia Polska* 2003; 58 (Supl. IV): 36-43.
21. Pluta W, Feusette P, Dzik G, et al. Ostre zespoły wieńcowe w województwie opolskim. Dane z ogólnopolskiego rejestru ostrych zespołów wieńcowych (PL-ACS). *Kardiologia Polska* 2005; 62 (Supl. I): 128-132.
22. White HD, Barbash GI, Califf RM, et al. Age and outcome with contemporary thrombolytic therapy. Results from the GUSTO-I trial. Global Utilization of Streptokinase and TPA for Occluded coronary arteries trial. *Circulation* 1996; 94: 1826-33.
23. A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. The Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO IIb) Angioplasty Substudy Investigators. *N Engl J Med* 1997; 336: 1621-8.
24. Zahn R, Schiele R, Schneider S, et al. Primary angioplasty versus intravenous thrombolysis in acute myocardial infarction: can we define subgroups of patients benefiting most from primary angioplasty? Results from the pooled data of the Maximal Individual Therapy in Acute Myocardial Infarction Registry and the Myocardial Infarction Registry. *J Am Coll Cardiol* 2001; 37: 1827-35.
25. Maślankiewicz K, Jaklik A, Jakubowski D, et al. Wyniki leczenia chorych z zawałem serca z uniesieniem odcinka ST w Górnośląskim Ośrodku Kardiologii w Katowicach. *Kardiologia Polska* 2003; 58 (Supl. IV): 19.
26. Jeger RV, Harkness SM, Ramanathan K, et al. Emergency revascularization in patients with cardiogenic shock on admission: a report from the SHOCK trial and registry. *Eur Heart J* 2006; 27: 664-70.
27. Hochman JS, Buller CE, Sleeper LA, et al. Cardiogenic shock complicating acute myocardial infarction – etiologies, management and outcome: a report from the SHOCK Trial Registry. Should we emergently revascularize Occluded Coronaries for cardiogenic shock? *J Am Coll Cardiol* 2000; 36: 1063-70.
28. Dauerman HL, Goldberg RJ, White K, et al. Revascularization, stenting, and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. *Am J Cardiol* 2002; 90: 838-42.
29. Barbash IM, Hasdai D, Behar S, et al. Usefulness of pre- versus postadmission cardiogenic shock during acute myocardial infarction in predicting survival. *Am J Cardiol* 2001; 87: 1200-3.
30. Gibson CM, Cannon CP, Murphy SA, et al. Relationship of TIMI myocardial perfusion grade to mortality after administration of thrombolytic drugs. *Circulation* 2000; 101: 125-30.
31. Waters RE 2nd, Mahaffey KW, Granger CB, et al. Current perspectives on reperfusion therapy for acute ST-segment elevation myocardial infarction: integrating pharmacologic and mechanical reperfusion strategies. *Am Heart J* 2003; 146: 959-68.
32. Hjalmarson A, Gilpin E, Kjekshus J, et al. Influence of heart rate on mortality after acute myocardial infarction. *Am J Cardiol* 1990; 65: 547-53.
33. Zuanetti G, Mantini L, Hernández-Bernal F, et al. Relevance of heart rate as a prognostic factor in patients with acute myocardial infarction: insights from the GISSI-2 study. *Eur Heart J* 1998; 19 (Suppl F): F19-26.
34. Pedersen OD, Abildstrom SZ, Ottesen MM, et al. Increased risk of sudden and non-sudden cardiovascular death in patients with atrial fibrillation/flutter following acute myocardial infarction. *Eur Heart J* 2006; 27: 290-5.
35. Steg PG, Goldberg RJ, Gore JM, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol* 2002; 90: 358-63.

Wpływ opóźnienia reperfuzji na wczesne wyniki leczenia chorych z ostrym zespołem wieńcowym z uniesieniem odcinka ST metodą pierwotnej angioplastyki wieńcowej

Ewa Trzos, Małgorzata Kurpesa, Zbigniew Bednarkiewicz, Jan Peruga, Jarosław Kasprzak, Michał Plewka, Barbara Uznańska, Maria Krzemińska-Pakuła

II Katedra i Klinika Kardiologii, Uniwersytet Medyczny, Łódź

Streszczenie

Wstęp: Wytyczne postępowania ACC/AHA oraz ESC zalecają pierwotną przezskórną interwencję wieńcową (pPCI) u chorych z zawałem serca z uniesieniem odcinka ST (STEMI) jako leczenie reperfuzyjne pierwszego rzutu, jeżeli można ją wykonać w czasie 90–110 min od pierwszego kontaktu z personelem medycznym. W grupach chorych leczonych metodą pPCI oceny dotyczące zależności między opóźnieniem reperfuzji a przeżyciem nie są nadal jednoznaczne.

Cel: Analiza wczesnych wyników leczenia STEMI metodą pPCI z uwzględnieniem czasu, jaki upłynął od początku objawów do rozprężenia balonu, oraz identyfikacja najważniejszych zmiennych wpływających na ryzyko wystąpienia złożonego punktu końcowego (zgonu, ponownego zawału serca czy udaru) we wczesnej, 30-dniowej obserwacji.

Metodyka: Badaną populację 1723 chorych podzielono na 4 grupy w zależności od czasu opóźnienia od początku bólu do pPCI. Grupa 1. to 311 chorych z opóźnieniem do 90 min, grupa 2. – 731 chorych z opóźnieniem 90–180 min, grupa 3. – 535 chorych z opóźnieniem 180–360 min, grupa 4. – 146 chorych z opóźnieniem >360 min.

Wyniki: Chorych przewożonych bezpośrednio z miejsca zamieszkania przez zespół pogotowia ratunkowego było 1175 (68,2%), natomiast 548 (31,8%) chorych transportowano z innych szpitali położonych zarówno w granicach miasta, jak i województwa. Średni czas transportu wynosił 54,5±17,8 min. Dla całej badanej populacji średni czas opóźnienia reperfuzji (od początku bólu do pPCI) wynosił 268,5±206 min, natomiast czas opóźnienia wewnątrzszpitalnego (drzwi–balon) wynosił 36,12±11,2 min. Nie stwierdzono istotnych różnic między badanymi grupami co do czasu opóźnienia wewnątrzszpitalnego. Na podstawie analizy danych demograficznych oraz klinicznych stwierdzono, że grupa 4. (z najdłuższym opóźnieniem od początku bólu) była najstarsza, przeważały w niej kobiety, częściej występowała u nich cukrzyca, zawał ściany przedniej oraz objawy niewydolności, w tym wstrząs kardiogeny. W tej grupie istotnie częściej ($p < 0,05$) stwierdzano zamknięcie gałęzi przedniej zstępującej (59%), pnia lewej tętnicy wieńcowej (6,2%) oraz wyższy odsetek pacjentów z wielonaczyniową chorobą wieńcową (53,2%). Zabieg PCI był skuteczny u 1649 (95,7%) chorych, przy czym u 85,5% uzyskano przepływ TIMI 3 i rezydualne zwężenie <30%. Najwyższy odsetek skutecznych udrożeń (98,3%) uzyskano w grupie 1. Stent lub stenty naczyniowe wszczepiono u 67,8% chorych, a leki blokujące receptor IIb/IIIa otrzymało 75,3% chorych. Odsetek wczesnych reokluzji w tętnicy dozawałowej był niewielki i wynosił 1,7%, przy czym częstość reokluzji i powtórnego zabiegu angioplastyki była istotnie wyższa w grupie 4. (11,6%). W trakcie obserwacji zmarło 70 (4,1%) chorych, przy czym najwyższy odsetek zgonów stwierdzono w grupie 4. (13,6%). Śmiertelność w okresie 30-dniowej obserwacji wynosiła 4,5%, a częstość innych zdarzeń sercowo-naczyniowych była następująca: ponowny zawał – 1,6%, udar mózgu – 0,7%, rewaskularyzacja – 2,2%. Z modelu wieloczynnikowego oceniającego ryzyko wystąpienia złożonego punktu końcowego wyodrębniono 4 niezależne zmienne mające wpływ na rokowanie: wiek, wstrząs kardiogeny, opóźnienie >6 godz., nieskuteczna PCI.

Wnioski: 1) Pierwotna przezskórną interwencja wieńcowa jest metodą leczenia STEMI pozwalającą uzyskać niską śmiertelność wewnątrzszpitalną (4,1%) i 30-dniową (4,5%). 2) Wczesne wyniki leczenia metodą pPCI, jak również wystąpienie złożonego punktu końcowego zależą od czasu opóźnienia reperfuzji, ale jego niekorzystny wpływ zaznacza się przede wszystkim u chorych z opóźnieniem >6 godz. 3) Pozostałe czynniki związane z wystąpieniem złożonego punktu końcowego to wstrząs, wiek >75 lat oraz skuteczność PCI.

Słowa kluczowe: ostry zespół wieńcowy, pierwotna angioplastyka, rokowanie

Kardiologia Polska 2007; 65: 1296–1304

Adres do korespondencji:

dr n. med. Ewa Trzos, II Katedra i Klinika Kardiologii, Wojewódzki Szpital Specjalistyczny, ul. Kniaźwiewicza 1/5, 91-347 Łódź, tel.: +48 42 251 60 34, e-mail: ewa_trzos@op.pl

Praca wpłynęła: 18.02.2007. Zaakceptowana do druku: 08.08.2007.