# Angiographic and clinical outcome after percutaneous coronary interventions following combined fibrinolytic therapy in acute myocardial infarction

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#### **Abstract**

**Introduction:** Combined therapy with fibrinolytic agent and platelet GPIIb/IIIa inhibitor not followed by an interventional procedure does not improve prognosis in patients presenting with acute ST-segment elevation myocardial infarction (STEMI) when compared to fibrinolysis alone. On the other hand, in the past percutaneous coronary interventions (PCI) performed after fibrinolysis were associated with low angiographic efficacy, a high risk of bleeding and a high rate of early cardiovascular events.

Aim: Evaluation of angiographic and clinical outcomes in patients with STEMI treated with PCI following combined fibrinolytic therapy

Methods and results: Complete angiographic and clinical data of 187 patients who underwent PCI immediately after combined fibrinolytic therapy were obtained from a survey of 669 consecutive patients with STEMI <12 hours, at age <75 years, without cardiogenic shock, who were transferred from regional hospitals to the catheterisation laboratory within 90 minutes and after the initiation of combined fibrinolytic therapy (alteplase 15 mg iv as a bolus followed by an infusion of 35 mg over 60 minutes; abciximab iv bolus of 0.25 mg/kg followed by a 12 h infusion of 0.125 μg/kg per minute; unfractionated heparin). At baseline angiographic examination revealed no flow (TIMI 0+1) in the infarct-related artery in 17.1% of patients, impaired flow (TIMI 2) in 17.1% and normal (TIMI 3) in 65.8% of cases. After immediate PCI, a significant improvement in epicardial perfusion (TIMI 2+3, 99.5%) and in microcirculation was achieved. This favourable effect was seen only in the group of patients with baseline TIMI 0+1 flow, whereas PCI in the group with baseline TIMI 3 flow did not cause any further improvement in microcirculatory perfusion. The rate of cardiovascular events within the first 30 days and 12 months after the procedures were similar in the studied subgroup of patients.

**Conclusions:** PCI performed after combined fibrinolytic therapy in STEMI patients is associated with high efficacy and improvement in indices of epicardial perfusion and microcirculation. These benefits are confined mainly to patients with primarily impaired flow in the infarction-related artery (TIMI 0+1). However, the clinical results of this strategy, particularly in patients undergoing PCI following successful combined fibrinolytic therapy, must still be proved in further randomised trials.

Key words: acute myocardial infarction, combined fibrinolytic therapy, facilitated coronary angioplasty

Kardiol Pol 2006; 64: 239-247

The purpose of reperfusion therapy in patients with acute ST-segment elevation myocardial infarction (STEMI) is an immediate and permanent flow restoration in the area supplied by the infarct-related artery (IRA) [1]. The most efficacious is primary percutaneous coronary intervention (PCI) which is regarded as method of choice in the management of STEMI in patients without an

anticipated delay of invasive therapy initiation, i.e. <90 minutes after the first medical contact [2]. The necessity of long transportation to a reference centre with 24/7 catheterisation lab availability may limit access to an invasive treatment for many patients with STEMI. In patients with an expected transfer delay time >90-120 minutes the method of choice is still

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fibrinolysis, which unfortunately is capable of restoring the patency of IRA only in about 60-80% of patients [3].

Currently, different approaches to STEMI management using both these methods, i.e. PCI preceded by fibrinolysis, to achieve early reperfusion during transfer (so-called facilitated PCI) are subject to clinical trials. In many of them, PCI for STEMI following fibrinolysis was found to be associated with low angiographic efficacy and a higher risk of haemorrhagic and ischaemic complications [4-6]. Nowadays, intracoronary stent implantation and intravenous platelet GPIIb/IIIa receptor blocker (GPIIb/IIIa blockers) administration improve PCI safety and efficacy, also in patients after an initial fibrinolytic therapy.

The aim of this study was to evaluate angiographic and clinical outcomes in patients with STEMI treated with PCI following combined fibrinolytic therapy.

# Methods

# Studied population

Complete angiographic and clinical data of 187 patients who underwent immediate PCI preceded by combined fibrinolytic therapy were obtained from a survey of 669 consecutive patients with STEMI treated within the Małopolska Programme of Myocardial Infarction Interventional Treatment, who were transferred to the Department of Haemodynamics and Angiocardiography, Institute of Cardiology in Kraków between June 2001 and June 2003 from community centres with an expected transfer time >90 min. Survey inclusion and exclusion criteria were described in detail in earlier reports [7, 8]. In short, it involved patients with STEMI <12 hours after the onset of pain, aged <75 years, without cardiogenic shock and without contraindications for combined fibrinolysis. All patients provided written consent prior to the proposed invasive treatment.

# Drugs used

In the emergency rooms of regional hospitals patients were given aspirin (325 mg), intravenous unfractionated heparin bolus (40 U/kg, maximum 3000 U), alteplase 15 mg and abciximab 0.25 mg/kg, followed by a continuous intravenous infusion of alteplase (35 mg over 60 min) and abciximab (12 h infusion of 0.125 µg/kg/min). Next, patients were transported by ambulance or by air to the Department of Haemodynamics and Angiocardiography of the Institute of Cardiology, Kraków. PCI procedures were performed by experienced interventional cardiologists as recommended by guidelines [2, 9, 10]. Complementary medical therapy was also prescribed according to clinical standards [2, 10].

#### Clinical assessment

The rate of serious coronary events, i.e. death, recurrent myocardial infarction, need for repeat urgent PCI or coronary artery bypass grafting, as well as of haemorrhagic complications during the follow-up at 30 days and 12 months were evaluated. Myocardial reinfarction was defined as a chest pain recurrence accompanied by new ECG changes (ST-segment elevation, left bundle branch block, new Q-wave) and/or a three-fold increase in kinase creatinine activity vs. baseline or a 50% above baseline activity if not within the normal range. Severe haemorrhagic complications were defined as bleeds causing haemodynamic compromise requiring transfusion. Moderate bleeding was defined as bleeding requiring blood transfusion but did not causing haemodynamic instability. The rate of minor haemorrhagic complications including the presence of haematoma at the arterial puncture site was also estimated. Haemorrhagic stroke occurence was assessed separately.

# Angiographic examination

An angiographic analysis was carried out in the referral centre of Kraków Cardiovascular Research Institute (Kraków, Poland) with the use of computer software New Quant32, QCAPlus (Sanders Data Systems, Palo Alto, CA, USA). The following parameters were evaluated: distal flow in IRA at baseline and after PCI by means of the TIMI scale, contrast medium inflow velocity according to the corrected number of TIMI frames (cTFC) and contrast flow through the myocardium on the myocardial perfusion scale (TMPG) [8, 11-13]. A complete assessment was performed in 187 patients who underwent immediate PCI following combined fibrinolytic therapy (appropriate quality of records, standard projections) according to generally accepted principles [8, 11-13].

# Statistical analysis

Corrected variables were expressed as the number and percentage of patients, continuous variables as a mean  $\pm$  standard deviation. Categorical variables were compared between groups by means of either chi-square or Fisher's exact test, while continuous variables were compared using either paired Student's t-test or nonparametric Kruskal-Wallis test. Two-tailed tests with the significance threshold of p $\leq$ 0.05 were used. Cumulative risk of death and rate of serious coronary events were estimated according to Kaplan-Meier curves and differences between treatment groups by means of log-rank tests.

#### Results

Among 669 patients, 557 underwent immediate PCI after combined fibrinolytic therapy while 108 patients were initially treated conservatively (Figure 1). During

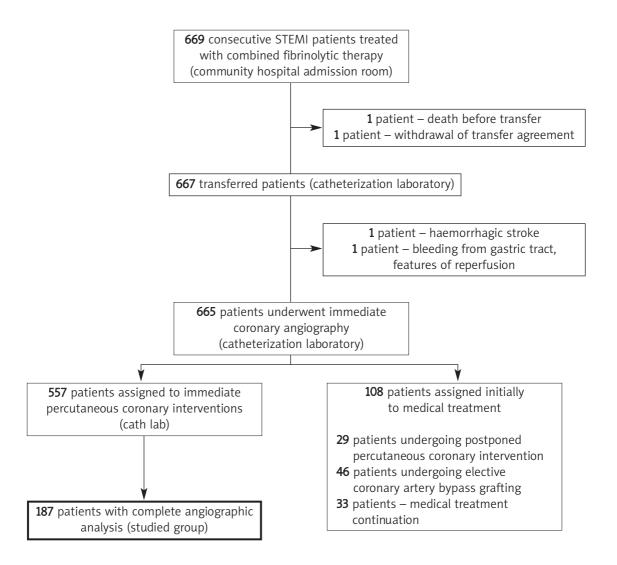


Figure 1. Scheme of group distribution in the survey

the 30-day follow-up, 19 (2.8%) deaths, 2 (0.3%) recurrent myocardial infarctions and 5 repeat PCI were noted. During 12-month follow-up, 27 (4.0%) deaths and 13 (1.9%) myocardial reinfarctions were seen and 29 (4.3%) patients underwent urgent PCI/coronary artery bypass grafting.

A definite analysis was carried out on 187 patients who underwent immediate PCI after combined fibrinolytic therapy with complete angiographic and clinical data (Figure 1). In the baseline angiographic study no flow (TIMI 0+1) in the infarct-related artery was seen in 32 (17.1%) cases, impaired flow (TIMI 2) in 32 (17.1%) and normal (TIMI 3) in 123 (65.8%) (Figure 2). For the above mentioned three subgroups of patients, angiographic parameters were evaluated and the rates of defined clinical endpoints were calculated.

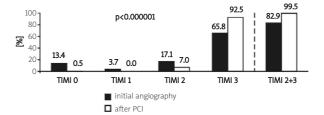


Figure 2. Flow in the infarct-related artery according to TIMI classification after combined thrombolysis in acute myocardial infarction noted in baseline angiography and angiography after PCI in the group of patients who underwent immediate PCI (n=187) (p <0.000001 for rate distribution difference for TIMI 0, 1, 2, 3 between studied groups)

**Table I.** Demographic and clinical data of patients in groups with baseline flow of TIMI 0+1, TIMI 2 and TIMI 3 in the infarct-related artery

	TIMI 0+1 in baseline angiography	TIMI 2 in baseline angiography	TIMI 3 in baseline angiography	p<
N=	32	32	123	
Age [years]	59.6±8.6	55.2±8.4	57.0±9.9	NS
Male gender	25 (78.1%)	22 (71.0%)	95 (76.6%)	NS
BMI [kg/m²]	26.4±3.3	27.4±3.3	27.0±3.8	NS
Diabetes	3 (9.4%)	5 (15.6%)	15 (12.2%)	NS
Arterial hypertension	17 (53.1%)	18 (56.3%)	62 (50.4%)	NS
Smoking	16 (50.0%)	18 (56.3%)	97 (78.9%)	0.004
History of ischaemic heart disease	16 (50.0%)	16 (50.0%)	49 (39.8%)	NS
History of myocardial infarction	7 (21.9%)	5 (15.6%)	11 (8.9%)	NS
Previous PCI	0 (0.0%)	0 (0.0%)	1 (0.8%)	NS
Previous CABG	0 (0.0%)	0 (0.0%)	1 (0.8%)	NS
Hyperlipidaemia	24 (75.0%)	25 (78.1%)	90 (73.2%)	NS
HR on admission [min <sup>-1</sup> ]	83±11	78±17	80±15	NS
SBP on admission [mmHg]	132±20	124±22	131±24	NS
DBP on admission [mmHg]	80±11	75±12	81±14	NS
Multivessel disease	15 (46.9%)	12 (37.5%)	68 (55.3%)	NS
IRA LAD	9 (28.1%)	19 (59.4%)	49 (39.8%)	
IRA Cx	6 (18.8%)	11 (34.4%)	60 (48.8%)	NS
IRA RCA	17 (53.1%)	2 (6.2%)	14 (11.4%)	
Time: pain onset to fibrinolysis [min]	247±145	192±98	233±141	NS

Abbreviations: (BMI – body mass index, PCI – percutaneous coronary intervention, CABG – coronary artery bypass grafting, HR – heart rate, SBP – systolic blood pressure, DBP – diastolic blood pressure, IRA – infarct-related artery, LAD – left anterior descending artery, Cx – circumflex artery, RCA – right coronary artery), IRA – infarct-related antery

Studied subgroups did not differ with respect to clinical and demographic characteristics (Table I), except for a higher percentage of smokers in the subgroup with normal flow in the IRA area. The rate of successful

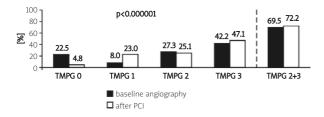


Figure 3. Microcirculatory flow in the area of the infarct-related artery according to the TMPG scale after combined thrombolysis in acute myocardial infarction found in baseline angiography and angiography after PCI in the group of patients who immediately underwent PCI (n=187) (p <0.000001 for rate distribution difference for TMPG 0, 1, 2, 3 between studied groups)

microcirculation reperfusion (TMPG 2+3) before the invasive procedure was significantly lower in the group with primary occluded IRA (Figure 3, Table II). PCI restored vessel patency in 99.5% of cases (Figure 2) and observed angiographic efficacy of the procedure was similar in different patient subgroups (Table II). Successful microcirculation reperfusion (TMPG 2+3) following PCI was observed in 72.2% of cases (Figure 3). Thus, significant improvement in epicardial and microcirculatory perfusion accompanied by a marked reduction of cTFC from 38±31 at baseline to 20±12 frames/second (p <0.00001) were noted as a result of immediate PCI performed after initial combined fibrinolytic therapy. An epicardial perfusion improvement (assessed by means of the TIMI scale) was found only in the group of patients with primary occluded IRA (TIMI 0+1) and with TIMI 2 flow at baseline (Table II). Additionally, PCI led to an improvement in microcirculatory reperfusion (TMPG) in the group of patients with primarily occluded IRA. PCI in the group with the baseline TIMI 3 flow did not lead to a significant epicardial perfusion deterioration. A reduction of mean cTFC was also

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	TIMI 0+1 flow in baseline angiography		TIMI 2 flow in baseline angiography		TIMI 3 flow in baseline angiography				
N=		32			32			123	
	before PCI	p<	after PCI	Before PCI	p<	after PCI	before PCI	p<	after PCI
TIMI 0+1 [%]	100.0		3.1	0.0		0.0	0.0		0.0
TIMI 2 [%]	0.0	0.000001	3.1	100.0	0.000001	28.1	0.0	NS	2.4
TIMI 3 [%]	0.0		93.8	0.0		71.9	100.0		97.6
cTFC [frames*s-1]	97±9	0.000001	24±18	47±17	0.000001	24±14	20±9	0.01	17±8
TMPG 0+1 [%]	81.3		56.3	37.5		28.1	14.7		18.7
TMPG 2 [%]	12.5	0.02	25.0	18.7	NS	34.4	33.3	NS	23.6
TMPG 3 [%]	6.2	-	18 7	43.8		37.5	52.0		57.7

**Table II.** Results of immediate PCI after combined thrombolysis in acute myocardial infarction assessed according to TIMI, cTFC and TNPG scales in groups of patients with baseline flow of TIMI 0+1, TIMI 2 and TIMI 3 (n=187) in the infarct-related artery.

observed but it was not associated with a marked microcirculatory reperfusion improvement (TMPG) (Table II).

The rate of haemorrhagic complications (30 days) and serious cardiovascular events within 30 days as well as 12 months were similar in the studied subgroups (Table III). Twelve-month Kaplan-Meier curves of both survival and freedom from coronary events are shown in Figures 4 and 5.

#### Discussion

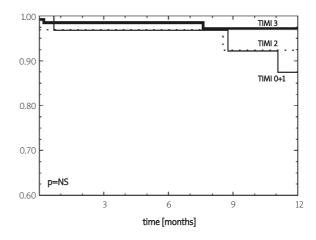
The use of half-dose fibrinolytic drug and full-dose GP IIb/IIIa blocker followed by PCI seems to combine the best aspects of the speed of fibrinolytic agent administration and PCI efficacy in STEMI. IRA patency restoration before PCI and time from the onset of chest pain to a complete reperfusion reduction may be associated with a better long-term prognosis for patients [14, 15]. On the other hand, there is a risk of haemorrhagic complications related to aggressive fibrinolytic therapy and ischaemic complications resulting from combined mechanical and pharmacologic methods of reperfusion.

# Angiographic efficacy of PCI

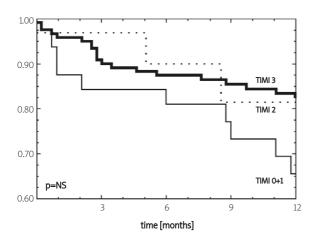
In 82.9% of examined patients, patent IRA (TIMI 3 flow in 65.8%) in the baseline angiographic examination was noted. The rate of patency observed herein is higher than in previously published reports of classical fibrinolytic treatment (IRA patency 60% to 80%) but similar to the results when combined therapy was used [3, 16-18].

In Topol et al.'s study and the TIMI IIA trial, PCI following fibrinolytic administration was associated with a lower efficacy than delayed PCI [5, 6]. On the other hand, Ross et al. showed that rescue PCI after failed fibrinolysis was not associated with a worse

angiographic outcome [19]. In our study, PCI after combined fibrinolytic therapy resulted in IRA patency in 99.5% of cases (including TIMI 3 flow in 92.5%), and PCI efficacy (TIMI 3 achievement) was similar in the groups with primarily occluded and patent IRA. These results are comparable with the results of primary PCI [20]. PCI preceded by combined fibrinolytic therapy led to either epicardial or microcirculatory perfusion improvement, particularly in patients with impaired epicardial flow. In the case of TIMI 3 flow in the IRA area, immediate PCI significantly reduced the mean value of cTFC. Importantly, the achievement of cTFC ≤20 frames/second corresponds to a lower risk of coronary events during follow-up and better systolic left ventricular function [11].



**Figure 4.** Twelve-month follow-up Kaplan-Meier survival curves of patients treated with facilitated PCI in acute myocardial infarction in subgroups of patients with baseline flow of TIMI 0+1 (continuous line), TIMI 2 (dotted line) and TIMI 3 (thickened line) in the infarct-related artery



**Figure 5.** Twelve-month Kaplan-Meier curves of freedom from cardiovascular events (death, recurrent myocardial infarction, repeat urgent coronary artery bypass grafting) of patients treated with facilitated PCI in acute myocardial infarction in subgroups of patients with baseline flow of TIMI 0+1 (continuous line), TIMI 2 (dotted line) and TIMI 3 (thickened line) in the infarct-related artery

# Clinical efficacy of PCI

PCI performed after classic fibrinolytic therapy in STEMI has been shown to be related to a significant increase in the number of ischaemic complications [4-6, 21, 22]. However, the use of antiplatelet drugs including aspirin was markedly limited at that time. Moreover, coronary stents improved the results of interventional treatment. The SIAM III, CAPITAL AMI and GARCIA-1 trials showed that PCI with coronary stent implantation following fibrinolytic treatment was associated with a reduction of ischaemic complications in comparison to the group of patients treated by means of delayed PCI or with PCI carried out depending on spontaneous/induced myocardial ischaemia onset. Thus, elective PCI after fibrinolysis seems to be justified to prevent IRA reocclusion which is related to left ventricular systolic performance deterioration and increased short- and long-term mortality [26, 27]. In contrast, the use of old fibrinolytic agents (streptokinase) preceding PCI increases the risk of ischaemic complications even with coronary stent implantation [28]. Moreover, PCI carried out after a highly fibrin-specific thrombolytic agent (tenekteplase) but without aggressive antiplatelet therapy may be associated with worse outcomes than

**Table III.** Rate of deaths, myocardial reinfarctions, urgent percutaneous coronary interventions (PCI), urgent coronary artery bypass grafting procedures (CABG) during the follow-up of 30 days and 12 months and haemorrhagic complications within 30 days in groups of patients with baseline flow of TIMI 0+1, TIMI 2 and TIMI 3 in the infarct-related artery. \* – a case of fatal haemorrhagic stroke <48 hours after the onset of the event (was included in the mortality analysis)

	TIMI 0+1 in baseline angiography	TIMI 2 in baseline angiography	TIMI 3 in baseline angiography	p<
N=	32	32	123	
Ischaemic complications within 30 days				
Death	1 (3.1%)	1 (3.1%)	2 (1.6%)	NS
Myocardial reinfarction	2 (6.2%)	0 (0.0%)	1 (0.8%)	NS
Repeat urgent PCI	1 (3.1%)	0 (0.0%)	1 (0.8%)	NS
Urgent CABG	0 (0.0%)	0 (0.0%)	0 (0.0%)	NS
Total number of cardiovascular complications	4 (12.4%)	1 (3.1%)	4 (3.2%)	NS
Ischaemic complications within 12 months				
Death	3 (9.4%)	2 (6.2%)	3 (2.4%)	NS
Myocardial reinfarction	4 (12.5%)	0 (0.0%)	4 (3.3%)	0.03
Repeat urgent PCI/CABG	3 (9.4%)	3 (9.4%)	13 (10.6%)	NS
Total number of cardiovascular complications	10 (31.3%)	5 (15.6%)	20 (16.3%)	NS
Haemorrhagic complications within 30 days				
Major haemorrhagic complications	0 (0.0%)	1 (3.1%)	5 (4.1%)	NS
Haemorrhagic stroke	0 (0.0%)	0 (0.0%)	1 (0.8%)*	NS
Moderate haemorrhagic complications	0 (0.0%)	0 (0.0%)	5 (4.1%)	NS
Minor haemorrhagic complications	6 (18.8%)	4 (12.5%)	15 (12.2%)	NS
Total number of haemorrhagic complications	6 (18.8%)	5 (15.6%)	26 (21.2%)	NS

after primary PCI, as demonstrated in the ASSENT-4 PCI trial – which was terminated early because of the high rate of ischaemic complications in the group of patients treated with PCI after initial fibrinolysis [29].

Further clinical improvement in outcome following STEMI may be the result of the additional use of GPIIb/IIIa receptor blockers. Their administration combined with a half-dose of highly fibrin-specific thrombolytic agent but not followed by an interventional therapy did not significantly reduce mortality. However, it resulted in reduction of risk of early IRA reocclusion reduction (i.e. recurrent myocardial infarction) in comparison to the group of patients treated with full-dose fibrinolysis, likely through the inhibition of fibrinolytic-induced platelet aggregation [30, 31]. Otherwise, the combination of the GPIIb/IIIa receptor blocker and streptokinase does not improve clinical outcome and additionally increases the risk of haemorrhagic complications [17].

PCI carried out after combined fibrinolytic treatment in the patient population presented herein had a high efficacy and did not lead to an increased rate of ischaemic complications. PCI following thrombolysis seems to be particularly justified in the case of initial therapy failure (the so-called rescue PCI). The study of Ross et al. and the REACT trial showed that rescue PCI was associated with a better clinical prognosis in comparison with the group of patients treated in a conservative manner or with an additional dose of a thrombolytic agent [19, 32]. However, obvious data indicating benefits of PCI immediately following fibrinolytic treatment, especially with flow TIMI 3 in the IRA area, are lacking. For instance, in Schweiger et al.'s study, PCI preceded by a successful combined fibrinolytic treatment was not associated with a higher risk of periprocedural complications and resulted in a reduction of hospitalisation time when compared to the group treated medically, but without a reduction in mortality [33]. On the other hand, there is a possibility to delay PCI after successful fibrinolytic therapy but it seems to be reserved particularly for combined therapy which indicates a lower rate of IRA reocclusions than observed in the case of full-dose fibrinolysis [30]. A definite answer to the question of the value of delayed PCI after successful combined fibrinolytic treatment in STEMI will be provided by ongoing CARESS in the AMI trial [34].

## Haemorrhagic complications

In the TIMI IIA, ECSG trials and O'Neill et al.'s study, an increased rate of major haemorrhagic complications and a necessity for blood transfusion were shown in a group of patients with PCI after fibrinolysis [4, 5, 21]. In recent studies the rate of haemorrhagic complications

after PCI preceded by fibrinolysis is not significantly higher than in patients treated medically or by means of delayed PCI [9, 17-19, 23-25]. It is mainly a result of heparin dose reduction, adjusted to the patient's weight and strict monitoring by ACT measurements [17]. The rate of haemorrhagic complications after combined fibrinolytic therapy in the studied group was similar to that observed in another studies using the same protocol [16, 17, 30].

# Summary

PCI performed after combined fibrinolytic therapy in STEMI correlates with a high PCI efficacy and an improvement in both epicardial and microcirculatory perfusion indices, but it is confined only to patients with primarily impaired flow in the IRA area. Routine PCI done to achieve optimal epicardial flow in the IRA area (TIMI 3) is safe but is not associated with a further angiographic improvement of myocardial reperfusion indices. Another randomised study is warranted to assess the clinical results of such a strategy.

#### References

- 1. Simes RJ, Topol EJ, Holmes DR Jr, et al. Link between the angiographic substudy and mortality outcomes in a large randomized trial of myocardial reperfusion. Importance of early and complete infarct artery reperfusion. GUSTO-I Investigators. *Circulation* 1995; 91: 1923-8.
- Van de Werf F, Ardissino D, Betriu A, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2003; 24: 28-66.
- Armstrong PW, Collen D. Fibrinolysis for acute myocardial infarction: current status and new horizons for pharmacological reperfusion, part 1. Circulation 2001; 103: 2862-6.
- Simoons ML, Arnold AE, Betriu A, et al. Thrombolysis with tissue plasminogen activator in acute myocardial infarction: no additional benefit from immediate percutaneous coronary angioplasty. *Lancet* 1988; 1: 197-203.
- Immediate vs delayed catheterization and angioplasty following thrombolytic therapy for acute myocardial infarction.
  TIMI II A results. The TIMI Research Group. JAMA 1988; 260: 2849-58.
- Topol EJ, Califf RM, George BS, et al. A randomized trial of immediate versus delayed elective angioplasty after intravenous tissue plasminogen activator in acute myocardial infarction. N Engl J Med 1987; 317: 581-8.
- Dudek D, Żmudka K, Kałuża GL, et al. Facilitated percutaneous coronary intervention in patients with acute myocardial infarction transferred from remote hospitals. *Am J Cardiol* 2003; 91: 227-9.
- 8. Dudek D, Bartus S, Żmudka K, et al. Assessment of myocardial reperfusion in patients with acute myocardial infarction treated with combination of fibrinolysis and IIb/IIIa platelet inhibitor. *Przegl Lek* 2002; 59: 1-6.

 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.

- 10. 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). Circulation 2004; 110: e82-292.
- Gibson CM, Murphy SA, Rizzo MJ, et al. Relationship between TIMI frame count and clinical outcomes after thrombolytic administration. Thrombolysis In Myocardial Infarction (TIMI) Study Group. Circulation 1999; 99: 1945-50.
- 12. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. TIMI Study Group. N Engl J Med 1985; 312: 932-6.
- 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.
- 14. De Luca G, Suryapranata H, Ottervanger JP, et al. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation* 2004; 109: 1223-5.
- De Luca G, Ernst N, Zijlstra F, et al. Preprocedural TIMI flow and mortality in patients with acute myocardial infarction treated by primary angioplasty. J Am Coll Cardiol 2004; 43: 1363-7.
- 16. Herrmann HC, Moliterno DJ, Ohman EM, et al. Facilitation of early percutaneous coronary intervention after reteplase with or without abciximab in acute myocardial infarction: results from the SPEED (GUSTO-4 Pilot) Trial. J Am Coll Cardiol 2000; 36: 1489-96.
- 17. Antman EM, Giugliano RP, Gibson CM, et al. Abciximab facilitates the rate and extent of thrombolysis: results of the thrombolysis in myocardial infarction (TIMI) 14 trial. The TIMI 14 Investigators. *Circulation* 1999; 99: 2720-32.
- 18. Califf RM, Topol EJ, Stack RS, et al. Evaluation of combination thrombolytic therapy and timing of cardiac catheterization in acute myocardial infarction. Results of thrombolysis and angioplasty in myocardial infarction-phase 5 randomized trial. TAMI Study Group. Circulation 1991; 83: 1543-56.
- Ross AM, Lundergan CF, Rohrbeck SC, et al. Rescue angioplasty after failed thrombolysis: technical and clinical outcomes in a large thrombolysis trial. GUSTO-1 Angiographic Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. *J Am Coll Cardiol* 1998; 31: 1511-7.
- 20. Schomig A, Kastrati A, Dirschinger J, et al. Coronary stenting plus platelet glycoprotein IIb/IIIa blockade compared with tissue plasminogen activator in acute myocardial infarction. Stent versus Thrombolysis for Occluded Coronary Arteries in Patients with Acute Myocardial Infarction Study Investigators. N Engl J Med 2000; 343: 385-91.
- 21. O'Neill WW, Weintraub R, Grines CL, et al. A prospective, placebo-controlled, randomized trial of intravenous

- streptokinase and angioplasty versus lone angioplasty therapy of acute myocardial infarction. *Circulation* 1992; 86: 1710-7.
- 22. SWIFT trial of delayed elective intervention v conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. SWIFT (Should We Intervene Following Thrombolysis?) Trial Study Group. *BMJ* 1991; 302: 555-60.
- 23. Le May MR, Wells GA, Labinaz M, et al. Combined angioplasty and pharmacological intervention versus thrombolysis alone in acute myocardial infarction (CAPITAL AMI study). *J Am Coll Cardiol* 2005; 46: 417-24.
- Scheller B, Hennen B, Hammer B, et al. Beneficial effects of immediate stenting after thrombolysis in acute myocardial infarction. J Am Coll Cardiol 2003; 42: 634-41.
- 25. Fernandez-Aviles F, Alonso JJ, Castro-Beiras A, et al. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. *Lancet* 2004; 364: 1045-53.
- 26. Gibson CM, Karha J, Murphy SA, et al. Early and long-term clinical outcomes associated with reinfarction following fibrinolytic administration in the Thrombolysis in Myocardial Infarction trials. *J Am Coll Cardiol* 2003; 42: 7-16.
- 27. Ellis SG, Debowey D, Bates ER, et al. Treatment of recurrent ischemia after thrombolysis and successful reperfusion for acute myocardial infarction: effect on in-hospital mortality and left ventricular function. *J Am Coll Cardiol* 1991; 17: 752-7.
- 28. Widimsky P, Groch L, Zelizko M, et al. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J 2000; 21: 823-31.
- 29. Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) Investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with STsegment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. *Lancet* 2006; 367: 569-78.
- 30. Topol EJ. Reperfusion therapy for acute myocardial infarction with fibrinolytic therapy or combination reduced fibrinolytic therapy and platelet glycoprotein IIb/IIIa inhibition: the GUSTO V randomised trial. *Lancet* 2001; 357: 1905-14.
- 31. Coller BS. GPIIb/IIIa antagonists: pathophysiologic and therapeutic insights from studies of c7E3. *Fab Thromb Haemost* 1997; 78: 730-5.
- 32. Gershlick AH, Stephens-Lloyd A, Hughes S, et al. Rescue angioplasty after failed thrombolytic therapy for acute myocardial infarction. *N Engl J Med* 2005; 353: 2758-68.
- 33. Schweiger MJ, Cannon CP, Murphy SA, et al. Early coronary intervention following pharmacologic therapy for acute myocardial infarction (the combined TIMI 10B-TIMI 14 experience). *Am J Cardiol* 2001; 88: 831-6.
- 34. Di Mario C, Bolognese L, Maillard L, et al. Combined Abciximab REteplase Stent Study in acute myocardial infarction (CARESS in AMI). *Am Heart J* 2004; 148: 378-85.

Wyniki angiograficzne i kliniczne przezskórnych interwencji wieńcowych po zastosowaniu kombinowanej terapii fibrynolitycznej w świeżym zawale serca

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## Streszczenie

**Wstęp:** Zastosowanie kombinacji fibrynolityku i blokera receptora płytkowego GpIIb/IIIa bez następowego leczenia interwencyjnego nie poprawia rokowania pacjentów ze świeżym zawałem serca z uniesieniem odcinka ST (STEMI) w porównaniu do leczenia wyłącznie litykiem. Z drugiej strony zabiegi przezskórnej interwencji wieńcowej (PCI) prowadzone po leczeniu fibrynolitycznym wiązały się w przeszłości z niską skutecznością angiograficzną, wysokim ryzykiem krwawień oraz wczesnych incydentów sercowo-naczyniowych.

**Cel:** Ocena wyników angiograficznych i klinicznych PCI po zastosowaniu kombinowanej terapii fibrynolitycznej u pacjentów z STEMI

**Metodyka i wyniki:** Z rejestru 669 kolejnych pacjentów z STEMI <12 godz., w wieku <75 lat, bez wstrząsu kardiogennego przekazywanych ze szpitali rejonowych z czasem transportu do pracowni hemodynamiki >90 min, po rozpoczęciu kombinowanego leczenia fibrynolitycznego (alteplaza bolus *i.v.* 15 mg, wlew *i.v.* 35 mg/60 min; abciksimab bolus *i.v.* 0,25 mg/kg, wlew *i.v.* 0,125 μg/kg/min przez 12 godz.; heparyna niefrakcjonowana) uzyskano pełne dane angiograficzne i kliniczne dla 187 pacjentów poddanych natychmiastowej PCI po kombinowanym leczeniu fibrynolitycznym. W wyjściowym badaniu angiograficznym brak przepływu (TIMI 0+1) w zakresie tętnicy odpowiedzialnej za zawał stwierdzono w 17,1% przypadków, przepływ upośledzony (TIMI 2) w 17,1% przypadków i przepływ pełny (TIMI 3) w 65,8%. W wyniku natychmiastowej PCI uzyskano istotną poprawę perfuzji nasierdziowej (TIMI 2+3 – 99,5%) oraz mikrokrążenia. Dotyczyła ona jednak jedynie grupy pacjentów z wyjściowym przepływem TIMI 0+1. Natomiast wykonanie PCI w grupie z wyjściowym napływem TIMI 3 nie prowadziło do dalszej poprawy perfuzji mikrokrążenia. Obserwowana częstość incydentów sercowo-naczyniowych w okresie 30 dni i 12 mies. była zbliżona w badanych podgrupach pacjentów.

Wnioski: Wykonanie PCI po zastosowaniu kombinowanej terapii fibrynolitycznej w STEMI wiąże się z wysoką skutecznością PCI oraz poprawą wskaźników pefuzji nasierdziowej i mikrokrążenia. Korzyść ta ograniczona jest jednak głównie do chorych z wyjściowo upośledzonym napływem do tętnicy odpowiedzialnej za zawał (TIMI 0+1) po zastosowaniu kombinowanej terapii fibrynolitycznej. Efekt kliniczny tej strategii postępowania, szczególnie dla grupy pacjentów poddanych PCI po skutecznym kombinowanym leczeniu fibrynolitycznym wymaga określenia w badaniach randomizowanych.

Słowa kluczowe: świeży zawał mięśnia sercowego, kombinowane leczenie fibrynolityczne, torowana angioplastyka wieńcowa

Kardiol Pol 2006; 64: 239-247

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Praca wpłynęła: 27.06.2005. Zaakceptowana do druku: 24.11.2005.