



SURVIVAL BENEFIT OF THE LATE PERCUTANEOUS CORONARY INTERVENTION IN THE PATIENTS AFTER ACUTE MYOCARDIAL INFARCTION WHO ARE OR WHO ARE NOT TREATED WITH THROMBOLYSIS

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ABSTRACT

The impact of late percutaneous coronary intervention (PCI) in the patients after acute myocardial infarction (AMI) on long term mortality remains to be established. At currently, thrombolysis is accepted as standard therapy when PCI is not immediately available. However, PCI is often performed in stable patients with AMI who are/are not received thrombolysis. We performed the trial that enrolled myocardial infarction patients treated with thrombolysis, late PCI and medically to assess the potential benefits of delayed PCI. We follow up 164 consecutive patients after AMI one year. The patients are divided in two groups; first group-66 patients who received reperfusion (37 patients received only thrombolysis, 10 patients received thrombolysis and PCI 7-9 days after thrombolysis and 19 patients underwent only PCI after 7-9 days) and second group-98 patients medically treated. One year mortality was 3% in the reperfusion group (2/66) and 14,3% in the medical group (14/98) ($p=0,016$). There were not significant differences between groups about other end points-reinfarctus, coronary artery bypass surgery and PCI performed later after discharge. The major predictors of one year mortality were ages ($p<0,001$) and ejection fraction ($p=0,003$). Also, therapy with beta-blockers ($p=0,002$), statins ($p=0,001$) and ACE-inhibitors ($p=0,024$) was associated with better survival. Delayed PCI performed 7-9 days after AMI in the patients who underwent thrombolysis or those did not improves outcome at long-term follow-up

KEY WORDS: PCI, thrombolysis, prognosis

INTRODUCTION

Many studies were demonstrated lowering of mortality after acute myocardial infarction (AMI) in the patients who were treated by thrombolysis shortly after AIM (during hospitalization or 30-days after AIM) (1). The salvaging of a jeopardized myocardium, patency of the infarct-related artery, microcirculatory perfusion, and myocytes preservation is consistent with the benefits achieved by reperfusion treatment (2). However, meta-analysis of the long-term benefits of intravenous thrombolytic therapy in more than 40000 patients participating in placebo-controlled trials shows that the risk of death after 1 month is equal in survivors of an AIM whether or not thrombolytic therapy was given irrespective of the time this treatment was started (based on data from the FTT Collaborative Group) (1). The GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) trial among the patients treated with different thrombolytic agents showed flow through the infarct-related artery was normal [Thrombolysis In Myocardial Infarction (TIMI) flow grade 3] in around 50 percent of them (3). The associations between patency of the infarct-related artery, better preservation of ventricular function, and improved survival after thrombolytic therapy for AIM suggests that only complete early reperfusion is associated with a reduced in-hospital mortality rate whereas patients with partial perfusion (TIMI grade 2) have a short-term prognosis similar to that of patients with persistently occluded infarct vessels (4). Also, myocardial contrast echocardiography (MCE) demonstrates that angiographically reflow cannot be used as an indicator of successful myocardial reperfusion in AMI patients (inadequate tissue reperfusion-“no reflow” phenomenon) (5). Other possible explanation may be higher incidence of rethrombosis and reinfarction in patients who received thrombolytic therapy after hospital discharge (6). However, other studies demonstrated that successful reperfusion and myocardial salvage produce significant mortality benefits that are amplified beyond the initial 30 days (7). Alternative treatment options of thrombolysis for coronary reperfusion in AIM is percutaneous coronary intervention (PCI). The DANAMI-2 trial showed that in patients with ST-elevation myocardial infarction (STEMI), a strategy of inter-hospital transfer for primary angioplasty was superior to on-site fibrinolysis at 30 days follow-up and the benefit of transfer for primary angioplasty based on the composite endpoint was sustained after 3 years (8). Also, a quantitative review of 23 randomised trials dem-

onstrated that patients treated by PCI had a significantly reduced likelihood of death, non-fatal reinfarction or stroke than those seen with thrombolytic therapy during long-term follow-up and whether or not the patient was transferred for primary PCI (9). In many developed countries, it is difficult to offer primary angioplasty to more than 20% to 30% of eligible patients (10). There are few studies comparing PCI with thrombolysis followed PCI. The nationwide study in France included 223 centres and 1714 patients over a 1-month period with 1-year follow-up was to assess outcomes in patients with AIM, with emphasis on comparing a pharmacoinvasive strategy (thrombolysis followed by routine angiography) with primary PCI (PPCI) concluded that a pharmacoinvasive strategy that combines thrombolysis with a liberal use of PCI yields early and 1-year survival rates that are comparable to those of PPCI (11). The meta-analysis of randomized trials comparing PCI of the infarct-related artery (>12 h to 60 days) with medical therapy in patients randomized >12 h after AMI showed a benefits of late PCI associated with significant improvements in cardiac function and survival (12). Current data support the strategy of immediate PCI after lytics than waiting for rescue PCI if lysis is non-effective (13). However, primary PCI is not offered at 50% of United States hospitals, and less in many other countries (14). The objective of this study was to investigate impact of both reperfusion therapy-fibrinolytic and late PCI on one-year prognosis in the patients with AIM.

METHODOLOGY AND PATIENTS

The 164 consecutive patients who were hospitalized during one year-from June, 2006 to June, 2007 with first AMI were followed-up one-year after discharge. Reperfusion therapy received 66 patients (group 1) -47 thrombolysis (37 only thrombolysis and 10 PCI after thrombolysis) and 19 were performed PCI. PCI was performed 7 to 9 days after AIM. The 98 patients were not eligible for thrombolytic therapy and did not performed PCI (group 2). Echocardiography (EHO) was performed at apparatus Philips HD 11 3-7 days from AMI. Troponin I was analyzed at apparatus Axsym (Abbott), creatine kinase and cholesterol at apparatus Beckman Sych 9. Coronarography was performed by usual technicians 5-7 days from AMI.

Statistical analysis

All analyzes were performed using SPSS 13.0 statistical software. Chi-square were used to determine the significance of the differences between mean values of baseline characteristics of the patients of the both

groups. Mann-Whitney test was used to compare EF between group. Survival curves were estimated by use of the Kaplan-Meier method. The significance of the difference between the survival curves was assessed by the log-rank test. Comparison of end points of patients with RT and those without RT was performed by relative risk estimate, Cox proportional-hazard regression models were used to determine variable into the model which had significant effect on survival. 2-tailed p values <0,05 were considered statistically significant.

RESULTS

Baseline Characteristics

The 164 consecutive patients with first AMI were follow-up one year after discharge from hospital. Of them, 47 patients (29%) received thrombolysis (37 only thrombolysis and 10 patients PCI after 7-9 days of thrombolysis) and only angioplasty 19 patients (12%). These 66 patients with reperfusion therapy represent group 1 and others 98 patients group 2. The baseline characteristics of the both groups are presented in Table 1. The patients of group 1 were younger (58,41 ±9,7 vs. 66,17±10,7, p<0,01) and men were treated with reperfusion therapy (RT) frequently than women (80% vs. 63%, p<0,05). The cardiac biomarkers, creatine kinase and troponins I were elevated significantly higher among the patients with RT (1691,6 vs. 1268,7, p<0,05 and 68,4 vs. 46,3, p<0,05). The patients treated with RT had frequently anterolateral Q wave AIM (32 /66-48% vs. 32/98-33% respectively, p<0,05). A part RT other therapy was not been different except furosemid which were been used less frequently among the patients treated with RT (15/66-23% vs. 42/98-43%, p<0,01).

Results of Coronary Angiography, Angioplasty and Echocardiography

Cardiac catheterization was carried out in the 30 patients with RT (30/47-63,8%) and in 53 patients without RT (53/117-45,3%). Among 30 patients who received RT 10 had occluded infarct arteries and 13 patients of these without RT (10/30-33,3% vs. 13/53-24,5% respectively). One occluded artery was reopened in the patients who were treated with RT. PCI was performed in 29 patients: the 10 patients with previously received thrombolysis and in the 19 patients without thrombolysis. The patients who received thrombolysis (early reperfusion) had significantly higher EF than those who did not (44,17 ±10,10 vs. 41,33±9,40, respectively, p=0,04) (Table 2). There was strongly correlation of concentration curve of Troponin I (Tn I) with low EF ≤40 area under the ROC (receiver operating characteristic) curve 0,606, 95% CI 0,517 – 0,696, p< 0,02.

Mortality

During follow-up, 2 patients (2/66-3%) in RT group died versus 14 (14/98-14,3%) in without RT group. One-year survival demonstrated by Kaplan Meier survival curves was much better (log rank -5,81, p=0,016) in the patients who underwent reperfusion (Figure 1). In the subgroup of 29 patients who were performed PCI all patients were survived, while 2 patients died among the 37 patients who were treated only with thrombolysis. One-year mortality risk modelling was performed with Cox regression model analysis which is identified age as the significant factor associated with increased mortality (p<0,001). Another factor influencing one-year mortality was EF (p=0,003). Also, Cox regression using For-

Characteristics	With reperfusion (n=66)	Without reperfusion (n=98)	P
Mean age, y	58,41±9,7	66,17±10,7	0,01
Male sex, %	80	65	0,05
Diabetes mellitus tipe 1	8	15	NS
Diabetes mellitus tipe 2	2	1	NS
Highest troponin I levels	68,4	46,3	0,05
Highest serum creatine kinase	1691,6	1268,7	0,05
Cholesterol	5,56	5,55	NS
Anterolateral Q wave AIM	32	32	0,05
Inferoposterior Q wave AIM	34	66	0,05
Beta blockers	53	67	NS
ACE-inhibitors	44	68	NS
Statins	56	77	NS
Furosemid	15	42	0,01
Digitalis	3	13	NS
Amiodarone	5	16	NS

AMI-acute myocardial infarction, ACE- angiotensin converting enzyme

TABLE 1. Baseline characteristics of the patients treated by reperfusion (thrombolysis or angioplasty) or did not.

Characteristics	With thrombolysis (n=47)	Without thrombolysis (n=117)	p
EDD	5,69±0,61	5,76 ±0,73	0,92
ESD	4,30±0,73	4,43 ±0,75	0,25
LA	3,92±0,54	4,01±0,58	0,47
EF,%	44,17±10,10	41,33±9,40	0,04
EF ≤40	17	49	0,59

EDD-end-diastolic diameter; ESD-end-systolic diameter; LA-left atrium diameter; EF-ejection fraction

TABLE 2. Results of Echocardiography

ward Stepwise selection method demonstrated among variables related to therapy that beta-blockers ($p=0,002$), statins ($p=0,001$) and ACE-inhibitors ($p=0,024$) were associated significantly to the survival time. Reinfarction had 3 patients in RT group (OD 0,936, 95% CI 0,390 to 2,349) and 4 patients in without RT group (OD 1,048, 95% CI 0,545 to 2,016). In the follow-up period 6 patients underwent PCI among the patients with RT (6/66-9,1%) and 14 patients who did not RT (14/98-14,1%). Coronary artery bypass graft surgery (CABG) after hospital discharge was performed in the 4 patients with RT (4/66-6,1%) and in the 7 patients among patients without RT (7/98-7,1%).

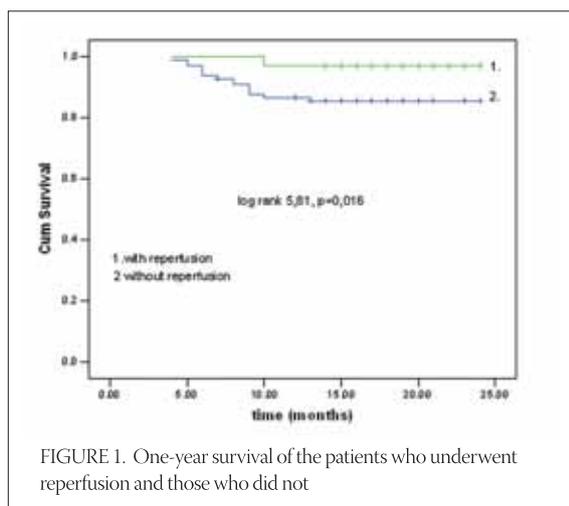


FIGURE 1. One-year survival of the patients who underwent reperfusion and those who did not

DISCUSSION

The principle aim for treatment of AMI is restoring coronary blood flow and reperfusing cardiac tissue achieving with thrombolysis or primary PCI. A prospective survey performed in Europe to examine adherence to current guidelines for ST elevation acute coronary syndromes the use of fibrinolytic therapy was 35,1% and 20,7% of primary PCI (15). In this study thrombolysis received 29 % of the patients, 6,1% PCI of them and 12 % late PCI only because availability of our centre does not offer 24 h/7 days primary PCI service. Baseline characteristics demonstrated that the patients with RT had frequently anterior AIM, higher peak concentration of cardiospecific enzymes that signi-

fies larger nekrosis of myocardium, but these patients were used much less diuretics suggesting good influence of reperfusion therapy on cardiac function.. That is also true because EF of left ventricle was statistically better in the patients who received thrombolysis than those who did not (44,17±10,10 vs. 41,33±9,40, $p=0.04$).

On the contrary to early reperfusion which reduce myocardial infarct size late reperfusion favourably affect infarct healing limit infarct expansion and limit LV remodelling (16). The patients with RT had much better survival than the patients without RF ($p=0,016$). The mechanisms proposed for benefit of late reperfusion which is known to reduce both cardiac remodelling and mortality and mitigates postinfarction remodelling is finding of granulation tissue cell proliferation which was increased to a greater degree in the patients who performed reperfusion (17). In the first large study which compare conservative and interventional therapy in patients who were subacute phase after AIM and single vessel disease overall mortality at follow up of 56 months was low, indicating a 2% risk per year but reduction in mortality from 11% to 4% with interventional therapy (18). Also, a prospective cohort of revascularisation patients within 14 days after AIM admitted to the coronary care units of 61 Swedish hospitals between 1995 and 1998 was obtained at 1 year mortality was 9,0% in the conservative group and 3,3% in the early revascularisation group (19). In our study Cox regression model analysis is identified ages ($p<0,001$), EF ($p=0,003$) and among variables related to therapy that beta-blockers ($p=0,002$), statins ($p=0,001$) and ACE-inhibitors ($p=0,024$) as the significant factors associated with increased mortality. In other study which was examined long-term (three years) prognosis in patients with AMI who underwent acute revascularization therapy advancing age was associated with increased mortality, also (20). The long term survival benefit in that study was demonstrated with more often the use of beta-blockers and ACE inhibitors in the patients with reperfusion therapy over three years period suggesting a better prevention of reocclusion and reinfarction and better preserved left ventricular function in patients treated with reperfusion therapy (20).

CONCLUSION

The late PCI performed in the subacute phase after an acute myocardial infarction, because rapid non availability and other problems with early PCI, alone or with thrombolysis shows an improvement in one-year survival of the patients after acute myocardial infarction. Therefore this study support concept of late open artery hypothesis

List of Abbreviations

AMI	-	acute myocardial infarction
PCI	-	percutaneous coronary intervention
TIMI	-	Thrombolysis In Myocardial Infarction
STEMI	-	ST-elevation myocardial infarction
PCCI	-	primary PCI
RT	-	reperfusion therapy
Tn I	-	Troponin I
CI	-	confidence interval
OR	-	odds ratio
EF	-	ejection fraction
LV	-	left ventricle
CABG	-	Coronary artery bypass graft surgery

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