

# Primary angioplasty in patients $\geq 75$ years old with ST-elevation myocardial infarction – one-year follow-up results

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## Abstract

**Background:** Efficacy and safety of primary percutaneous coronary angioplasty (PCI) in elderly patients with acute ST-elevation myocardial infarction (STEMI) have not yet been definitely established because these patients were usually excluded from large randomised trials.

**Aim:** To evaluate in-hospital and one-year outcome after primary PCI in elderly patients, and to assess clinical characteristics of this group.

**Methods:** The study population included 1061 consecutive STEMI patients, mean age  $60.6 \pm 17$  years, treated with primary PCI. Clinical characteristics and results of 127 patients aged  $\geq 75$  years were compared to the younger group.

**Results:** Elderly patients were more frequently female (48.4 vs. 23.6%,  $p < 0.005$ ) and diabetics (22.2 vs. 12.1%,  $p < 0.02$ ) and more frequently had renal and/or left ventricular failure (22.3 vs. 9.1%, and 9.1 vs. 4.5%,  $p < 0.005$ , respectively). In older patients less frequently stents were implanted and TIMI flow 3 was restored (65.1 vs. 78.8%,  $p < 0.05$  and 74.6 vs. 84.7%,  $p < 0.03$ ). In-hospital mortality in older versus younger patients was 11.8 vs. 3.0%,  $p < 0.005$ . The incidence of in-hospital complications (stroke, major bleeding and reinfarction) was similar in both groups. The one-year mortality and MACE rates were higher in older patients (21.3 vs. 6.0% and 24.9 vs. 11.0%,  $p < 0.0005$ ). In multivariate analysis Killip class II-IV (OR 6.73; 95% CI 1.75-25.97,  $p = 0.006$ ) and heart rate (OR 1.04; 95% CI 1.01-1.07,  $p = 0.03$ ) were independent predictors of one-year mortality in patients aged  $\geq 75$  years.

**Conclusions:** Primary PCI in older STEMI patients is associated with a favourable in-hospital and one-year outcome, although inferior to that seen in younger patients. The in-hospital complication rate is similar in the elderly and in younger patients.

**Key words:** STEMI, primary angioplasty, prognosis, elderly patients

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## Introduction

Acute myocardial infarction (MI) is a leading cause of death and morbidity in older patients in developed countries. According to the Swedish National Acute Myocardial register during 1987-1995, one-year mortality in patients  $\geq 75$  years old was over 50% [1]. Despite wide implementation of reperfusion therapy in recent years, due to systematic exclusion of older patients from many randomised trials, the benefits and complications of both primary percutaneous coronary intervention (PCI) and fibrinolysis in older people remain controversial [2-4]. In elderly patients, fibrinolysis may carry a higher risk of stroke and major bleeding, whereas primary PCI might be associated with a higher risk of periprocedural complications and a lower rate of reperfusion [5, 6]. Randomised clinical trials and observational

studies suggest that in elderly patients primary PCI is more effective than pharmacological reperfusion [7-11]. Thiemann et al. showed that thrombolytic therapy in patients with myocardial infarction older than 75 years might even be associated with survival disadvantage [12].

The aim of the study was to evaluate in-hospital and one-year results of primary PCI in ST-elevation myocardial infarction (STEMI) patients aged 75 years and older, treated in a high-volume invasive centre, and to assess clinical characteristics of this group.

## Methods

A total of 1061 consecutive patients (mean age  $60.6 \pm 17$ , range 31-96 years), with STEMI treated with primary PCI within 12 hours from the onset of chest pain were analysed.

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All data were collected in a prospective registry [13]. The study protocol was approved by the local Ethics Committee. Primary PCI procedures were performed by an experienced team at a high-volume centre with a 24-hour invasive service. All patients were treated with a loading dose of aspirin (300-500 mg), clopidogrel (300 mg), and single dose of heparin (70-100 U/kg), followed by a typical daily dosing of aspirin, and clopidogrel or ticlopidine. The use of abciximab was left to the discretion of the operator, however, it was electively administered in patients with anterior STEMI or diabetes. The STEMI and cardiogenic shock criteria were described previously [14, 15].

In-hospital and one-year clinical course of patients studied was evaluated using the hospital files, telephone calls, mailed questionnaire and National Citizen Registry (PESEL).

Major adverse cardiac events (MACE) were defined as combined occurrence of death, stroke or MI.

### Statistical analysis

Results are presented as means  $\pm$ SD or medians for continuous variables, and as percentages for categorical data. Groups were compared (all tests two-sided) by unpaired t-test or Mann-Whitney-Wilcoxon test depending on normality of distribution. Frequencies were compared using chi-square or Fisher's exact test. A multivariate logistic regression model was used to test the association

of baseline variables with the end point of death in one year for patients aged  $\geq 75$  years. The final model included: age, gender, Killip class II-IV, heart rate, creatinine level, systolic blood pressure, pain-to-balloon time, stent implantation, diabetes, history of MI, localisation of recent MI, elective use of abciximab, and TIMI 3 flow after the procedure. Statistical analysis was performed using SPSS for Windows 9.0 software.

### Results

Out of the whole study group, 127 (12%) patients were aged  $\geq 75$  years. Baseline clinical characteristics are listed in Table I. Three patients from the younger group were lost

**Table I.** Baseline characteristics (1061 patients)

	Age $\geq 75$ years n=127	Age <75 years n=934	p
Female gender	61 (48.4%)	220 (23.6%)	<0.0005
Arterial hypertension	76 (59.5%)	467 (50.5%)	NS
Diabetes	28 (22.2%)	113 (12.1%)	<0.001
Creatinine >133 [ $\mu$ m/l]	28 (22.3%)	85 (9.1%)	<0.0005
History of MI	38 (29.7%)	188 (20.1%)	<0.02
Recent anterior MI	44 (34.4%)	371 (39.7%)	NS
Multivessel disease	74 (58.7%)	489 (52.4%)	NS
Killip class II-IV	32 (9.1%)	98 (10.5%)	<0.0005

**Table II.** Primary PCI data, in-hospital and one-year results

	Age $\geq 75$ years n=127	Age <75 years n=934	p
<b>Periprocedural data</b>			
Pain-to-balloon time [hours]	5.4 $\pm$ 2.6	4.4 $\pm$ 2.3	<0.0005
Stent implantation	83 (65.4%)	736 (78.8%)	<0.001
Abciximab	49 (38.6%)	450 (48.2%)	<0.004
TIMI 3 flow after procedure	94 (74.0%)	790 (84.6%)	<0.03
CK max [U/l]	2129 $\pm$ 2281	1943 $\pm$ 1999	NS
IABP	4 (3.2%)	15 (1.7%)	NS
<b>In-hospital events – whole group</b>			
Death	15 (11.8%)	28 (3.0%)	<0.005
Stroke	1 (0.8%)	6 (0.6%)	NS
Major bleeding	6 (5.0%)	31 (3.3%)	NS
Reinfarction	2 (1.7%)	14 (1.5%)	NS
<b>In-hospital events – patients with cardiogenic shock</b>			
death	8 (73.0%)	14 (43.7%)	<0.0001
<b>One-year events – whole group</b>			
MACE	29 (24.9%)	95 (11.0%)	<0.0005
Death	27 (21.3%)	56 (6.0%)	<0.0005
<b>One-year events – patients with cardiogenic shock</b>			
Death	8 (73.0%)	15 (48.4%)	<0.0001

Abbreviations: CK – creatine kinase, IABP – intra-aortic balloon pumping, MACE – major adverse cardiac events (death, stroke, MI)

**Table III.** Independent predictors of one-year mortality in patients aged 75 years and older (n=127)

	OR	95% CI	P
Killip class II-IV	6.73	1.75-25.97	0.006
Heart rate	1.04	1.01-1.07	0.03

to follow-up. Patients aged  $\geq 75$  years as compared to younger were more frequently female and diabetics. They experienced more frequently: renal and severe left ventricular failure (22.3 vs. 9.1%,  $p < 0.005$  and 9.1 vs. 4.5%,  $p < 0.005$ , respectively). No significant differences were found between study groups in the incidence of arterial hypertension, anterior localisation of recent MI or multivessel disease.

Primary PCI data, in-hospital and one-year results are summarised in Table II. Time from the onset of symptoms to reperfusion was longer in older patients. During primary PCI procedures in older patients stents were significantly less frequently implanted, and TIMI flow 3 was less frequently restored in comparison to controls. In-hospital mortality was nearly four times higher in patients aged  $\geq 75$  years as compared to younger ones despite the similar MI size and similar use of intra-aortic balloon pumping. The incidence of severe post-procedural complications (stroke, major bleeding and reinfarction) was similar in older and younger patients. The one-year mortality and MACE rates were statistically significantly higher in patients  $\geq 75$  years old.

We analysed also the outcome of patients aged  $\geq 75$  years with cardiogenic shock (Table II). Both the in-hospital and one-year mortality were 73.0%. This means that no patient from this group died after discharge from hospital during one year.

In a multivariate logistic regression model (Table III), only Killip class II-IV (OR 6.73; 95% CI 1.75-25.97,  $p=0.006$ ) and heart rate (OR 1.04; 95% CI 1.01-1.07,  $p=0.03$ ) were identified as independent predictors of mortality in the older group during the follow-up. Other analysed factors (age, gender, systolic blood pressure, diabetes, creatinine level, history of MI, localisation of recent MI, pain-to-balloon time, stent implantation, elective abciximab administration, TIMI 3 flow after the procedure) did not contribute significantly to the model.

## Discussion

Patients aged 75 years and older comprise the majority of patients who die and nearly 40% of those who are admitted to hospitals due to MI [16, 17]. Due to under-representation in clinical trials and fear of treatment-induced complications, primary PCI is implemented with caution in this group and treatment of

these very high-risk patients depends on an individual approach and the experience of the physician [2-4].

Our study demonstrated differences between older (aged  $\geq 75$  years) and younger patients with STEMI treated by primary PCI in presentation, invasive treatment, early outcome and one-year results. We found a significant increase in mortality and MACE in elderly patients despite the similar MI size and localisation, and similar incidence of multivessel disease. In multivariate analysis only Killip class II-IV and heart rate were identified as independent predictors of one-year mortality. In fact, both these factors are clinical signs of heart failure.

Like other authors we found that patients aged  $\geq 75$  with acute MI had a different profile than the younger group [11, 12]. They were referred later to hospitals. They were more likely to be women, diabetics, to have a history of MI, and left ventricular failure on admission.

Important questions are: do differences in baseline, procedural characteristics explain the difference in prognosis between older and younger patients with STEMI? Should stents and abciximab in older patients be used based on the same principles as in younger ones?

Primary angioplasty is only a final part in the integrated emergency care of AMI patients. The outcome of invasive treatment, especially in high-risk patients, depends much on fast and competent pre-hospital procedures. The one-hour delay in pain-to-balloon time observed in our study group confirms other reports, and shows what should be changed in the future. More attention should be focused on early recognition of MI in seniors and rapid transfer to an invasive centre. Such an approach seems to be the best way to reduce the development of decompensated heart failure (Killip class II-IV) and increased heart rate prior to primary PCI. Also, immediate and proper administration of aspirin, anticoagulants and clopidogrel, when not contraindicated, should be mandatory.

In the older group we used fewer stents and abciximab, and normal TIMI 3 flow was less frequently obtained (Table II), but unlike data from the literature, in multivariate analysis these factors had no independent negative significance [18]. Moreover, in contrast to previous reports in our older patients we found no increase in in-hospital complications [19]. To comment on these interesting findings, in our series the balance between optimal angiographic result and fear of complications was presumably oriented to avoid major periprocedural complications, which are known to be especially life threatening in the older population. A new anticoagulant, fondaparinux, seems to have a favourable safety/efficacy profile, and after further evaluation may become especially valuable in the older population [20]. Our results also confirm that in older patients an individual approach and operator experience are still more important than in the younger group.

Mehta et al. in the GRACE registry, analysing nearly 3,000 patients  $\geq 70$  years of age with STEMI, found that, compared with patients receiving thrombolysis, those treated with primary PCI had lower in-hospital mortality (14.4 vs. 17.6%; adjusted OR 0.62; 95% CI 0.39-0.69), reinfarction rates (1.0 vs. 5.7%,  $p=0.003$ ), and a trend toward lower rates of stroke (1.1 vs. 2.8%,  $p=0.08$ ), but also a trend for higher major bleeding rates (8.6 vs. 5.9%,  $p=0.09$ ) [10]. The National Registry of Myocardial Infarction investigators found a lower rate of combined end point of death and stroke in patients  $\geq 75$  years of age with STEMI treated with primary PCI vs. alteplase [21]. Based on our results and those from the literature one can suggest that stents should be implanted using the same criteria and frequency as in younger patients. In the case of abciximab administration the benefit seems less evident. Attention should be paid to the presence of contraindications and possible higher complication rate.

In-hospital mortality in older patients with STEMI complicated by cardiogenic shock is up to 90%, and these patients were excluded from almost all trials and observational studies. The SHOCK randomised trial reported no benefit in six-month mortality in patients  $\geq 75$  years of age in the emergency revascularisation approach versus initial medical stabilisation [22]. In contrast, the non-randomised SHOCK registry found a marked survival benefit with late versus no revascularisation. Our results show a favourable one-year prognosis in older patients with STEMI complicated by cardiogenic shock treated by primary PCI, who survived to hospital discharge.

### Study limitations

Some high-risk elderly patients may not have been referred to an invasive centre. We should also remember that the majority of MI deaths are pre-hospital deaths. Another limitation is that the results of a single centre study may be influenced by patient selection biases.

### Conclusions

STEMI patients aged  $\geq 75$  years represent a different clinical profile with higher rates of comorbidities than the younger group. Primary PCI performed by an experienced team in a high-volume centre does not cause a significant increase in acute peri-procedural complications such as stroke, major bleeding and reinfarction. The symptoms of Killip class II-IV heart failure and accelerated heart rate prior to primary PCI are independent predictors of one-year mortality in elderly patients. Those aged  $\geq 75$  years with STEMI complicated by cardiogenic shock treated by primary PCI have good one-year prognosis, once they have survived the acute phase.

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# Pierwotna angioplastyka wieńcowa u chorych $\geq 75$ . roku życia z zawałem serca z uniesieniem odcinka ST – wyniki rocznej obserwacji

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## Streszczenie

**Wstęp i cel:** Starsi chorzy byli systematycznie wyłączeni z większości wieloośrodkowych badań klinicznych, na podstawie których opracowano obowiązujące standardy leczenia zawału serca. Celem pracy jest ocena rocznych wyników leczenia metodą pierwotnej angioplastyki wieńcowej (PCI) osób w wieku 75 lat i starszych oraz poszukiwanie charakterystyki klinicznej tej grupy.

**Metodyka:** Analizie poddano grupę 1061 kolejnych chorych z ostrym zawałem serca z uniesieniem odcinka ST (STEMI), w wieku średnio  $60,6 \pm 17$  lat, leczonych metodą pierwotnej PCI. Badaną grupę stanowiło 127 osób w wieku 75 lat lub więcej, których charakterystykę kliniczną, przebieg wewnątrzszpitalny oraz roczne wyniki porównano z pozostałymi chorymi.

**Wyniki:** W grupie osób starszych było więcej kobiet (48,4 vs 23,6%,  $p < 0,005$ ), chorych na cukrzycę (22,2 vs 12,1%,  $p < 0,02$ ), chorych z niewydolnością nerek (22,3 vs 9,1%,  $p < 0,005$ ) i niewydolnością serca (9,1 vs 4,5%,  $p < 0,005$ ). U starszych chorych rzadziej implantowano stenty i rzadziej uzyskiwano przepływ TIMI 3 (odpowiednio: 65,1 vs 78,8%,  $p < 0,05$  i 74,6 vs 84,7%,  $p < 0,03$ ). Śmiertelność wewnątrzszpitalna była istotnie wyższa u osób starszych niż w pozostałej grupie (11,8 vs 3,0%,  $p < 0,005$ ). Częstość wewnątrzszpitalnych zdarzeń niepożądanych (udar mózgu, poważne krwawienia, ponowny zawał) była porównywalna w obu grupach. Roczna śmiertelność i częstość poważnych zdarzeń sercowo-naczyniowych (MACE) była istotnie większa wśród osób starszych (odpowiednio: 21,3 vs 6,0% i 24,9 vs 11,0%,  $p < 0,0005$ ). W analizie wieloczynnikowej jedynie częstotliwość akcji serca przy przyjęciu (OR 1,04; 95% CI 1,01–1,07,  $p = 0,03$ ) i II–IV klasa wg Killipa (OR 6,73; 95% CI 1,75–25,97,  $p = 0,006$ ) były niezależnymi predyktorami rocznej śmiertelności u osób w wieku 75 lat i więcej.

**Wnioski:** Pierwotna angioplastyka wieńcowa u starszych osób jest skuteczną metodą leczenia STEMI, a wykonana przez doświadczony zespół nie wiąże się ze wzrostem częstości powikłań. Chorzy w wieku 75 lat i więcej ze STEMI powikłanym wstrząsem kardiogenym, którzy przeżyli okres szpitalny, mają korzystne rokowanie roczne.

**Słowa kluczowe:** pierwotna angioplastyka, rokowanie, osoby starsze

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