Myocardial infarction in the elderly. Clinical and therapeutic differences

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Abstract

Background: The progressive aging of society results in increased numbers of acute myocardial infarctions (MI) in the elderly. In the presence of huge progress in MI treatment, it seems to be reasonable to analyse clinical course and prognosis in the elderly with MI.

Aim: To assess differences in clinical characteristics and treatment of MI between patients younger than 65 and the elderly.

Methods: A total of 491 patients over 65 and 398 patients younger than 65 with acute MI between June 2005 and February 2006 were retrospectively analysed.

Results: In patients over 65 there was significantly higher prevalence of arterial hypertension and diabetes, as well as low left ventricular ejection fraction and advanced heart failure. The time from onset of symptoms to admission was longer in the older group. The rate of reperfusion therapy in the elderly was significantly lower, and the results of invasive treatment were poor. Antiplatelet treatment was less aggressive in this group. In-hospital and long-term mortality were significantly higher in patients over 65, but the lowest in subjects undergoing invasive strategy.

Conclusions: Risk factors in baseline characteristics and lower rate of invasive therapeutic strategy result in worse prognosis in patients over 65 with acute MI. A significant reduction in mortality due to the invasive approach should encourage wide implementation of this approach in the elderly.

Key words: myocardial infarction, elderly, reperfusion therapy

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Introduction

The incidence of myocardial infarction (MI) increases with age. The definition of older age is not clear. The majority of authors determined 70 years as a cut-off age for this population, although some suggest 65 or 75 years of age. Besides, senility is perceived to be relative as the registered age does not always relate to the biological one. According to the WHO classification, people aged 60-75 years are referred to as elderly subjects, 75-90 years as senile and above 90 years as the oldest age group. At present in the US the classification into young-old at the age of 65-75 and old-old at >75 years of age is valid [1].

In Poland the notion of advanced age is usually used to characterise people between 65 and 75 years, senile age refers to the age range from 75 to 85 and >85 years of age is called old age. People from the oldest age group are also defined as long-lived [2].

The assessment of MI therapy progress in older people seems to be of great importance in the light of reports on aging processes of societies associated with improvement of the economic status together with much better healthcare services in many countries worldwide. Currently, people aged >65 years constitute 13% of the entire US population, accounting for 60% of all MI cases and 88% of all MI-related deaths. Similarly, people aged 75 years or more, making up only 5% of the US population, accounted for 34% of all MIs and 45% of MI-related deaths [3].

In Poland, the population of older people is also constantly increasing in number and in 2020 is forecast to constitute 24% of the entire population, compared to 16% in 1995. The most prominent population growth is currently

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observed because the post-war age group of population boom has been entering into the older age group since 2005. In the coming 5-year period this population growth will be oscillating around one million people [4].

It has been known for a long time that the atherosclerotic process grows worse with age. Nevertheless, only in recent years have studies evaluating the influence of aging on myocardial metabolism been published. It turned out that fatty acid metabolism decreased with age whereas the myocardial use of glucose remained unchanged. Thus, in comparison with fatty acids it brings about a relative increase in glucose consumption as an energetic substrate. Less dependence of myocardial cells on fat metabolism seems to lead to lesser myocardial susceptibility to ischaemia in older age, which is beneficial. Such a shift of metabolism can be associated with pathological situations as well. Similar metabolic changes were also reported in left ventricular (LV) hypertrophy and dilated cardiomyopathy [5].

The body's aging affects vascular endothelium as well. Over the years progressive impairment of nitrogen oxide is observed [6]. Moreover, aging of smooth muscles of the vascular walls results in weaker vasomotor response to other vasomotor factors [7]. Due to more frequent coexistence of concomitant diseases in older people which impair the function of endothelium to an even greater extent, atherosclerotic lesions in this population are more often present and disseminated, and additionally affect many vessels as well as encompass their peripheral segments, which hinders revascularisation in many cases.

In view of the enormous progress in MI treatment at the turn of the 20th/21st century, a separate analysis of clinical course and prognosis in older people appears to be essential.

Methods

Study group

Retrospective analysis of clinical course and long--term prognosis was carried out in 889 patients hospitalised due to MI from June 2005 to February 2006. Among all individuals a group of 491 older patients (>65 years old) and a group of 398 younger ones (≤65 years old) were selected.

The study inclusion criterion in both populations was ST elevation at J point above 0.2 mV in leads V_1–V_3 and/or above 0.1 mV in the remaining leads (in at least two leads corresponding with a target wall) together with typical increase in cardiac necrosis biomarkers troponin T and/or CK-MB.

Long-term follow-up

Data regarding in-hospital MI course were gained from the Polish Register of Acute Coronary Syndromes PL-ACS, whereas information on long-term prognosis (6-month follow-up) was worked out based on statistics of the Registry Office and National Health Fund Department.

Statistical analysis

Continuous variables are presented as the mean ± standard deviation or median and interquartile interval, depending on distribution. The significance of differences between means was tested with Student's t test or U Mann-Witney tests. Qualitative parameters were compared using χ^2 test. If the expected frequency was <5, Yates' correction was used. Six-month mortality was analysed with Kaplan-Meier statistics and the significance of differences between groups with log-rank test. Multivariable analysis of in-hospital and 6-month mortality was carried out using multivariable logistic regression and showing results as the odds ratio (OR) and 95% confidence interval (CI). Results were found statistically significant if $p \leq 0.05$ (two-sided). Calculations and statistical analyses were performed using Statistica PL software ver. 6.1 (StatSoft Inc.).

Results

Mean age of older subjects hospitalised due to MI was 75.7±6.3 years, and in the younger group 54.2±7.3 years. A much higher percentage of women among older patients compared to younger ones was observed. In addition, in older patients a significantly higher incidence of diabetes and hypertension was reported; on the other hand, abnormal lipid profile and smoking were observed rarely in older subjects (Table I).

In the older group, LV ejection fraction (LVEF) was significantly lower and the number of patients with heart failure in Killip-Kimball class II-IV was significantly higher.

Table I. Clinical characteristics of older patients (aged >65 years) and younger ones (aged ≤65 years) hospitalised from June 2005 to February 2006 (N=889)

Variable	Subjects aged ≤65 n=398 (44.7%)	Subjects aged >65 n=491 (55.2%)	p
Age [years]	54.2±7.3	75.7±6.3	<0.0001
Females [%]	20.1	46.6	<0.0001
Past myocardial infarction [%]	14.8	16.1	0.60
Diabetes mellitus [%]	13.8	23.0	0.0005
Hypertension [%]	58.0	69.0	0.0007
Lipid disturbances [%]	62.6	49.1	<0.0001
Smoking [%]	56.0	15.1	<0.0001

Table II. Comparison of myocardial infarction course between two age groups: ≤65 years old and >65 years old (N=889) [%]

Variable	Subjects aged ≤65 n=398 (44.7%)	Subjects aged >65 n=491 (55.2%)	p
Location of myocardial infarction			
anterior	35.9	41.3	0.10
inferior	54.3	44.8	0.0050
other	9.8	13.9	0.065
Conduction disturbances			
right bundle branch block	3.3	4.5	0.35
left bundle branch block	0.8	4.9	0.0004
Killip-Kimball class on admission			
1	73.4	57.0	<0.0001
2	18.3	26.7	0.0033
3	2.3	6.5	0.0026
4	6.0	9.8	0.042
Left ventricular ejection fraction [%] (n=672)			
reference ranges	33.1	18.1	<0.0001
40-50%	53.5	56.6	0.42
20-40%	12.8	23.6	0.0003
<20%	0.6	1.7	0.31
Time from pain to hospital admission			
0-4 h	57.2	48.3	0.008
>4 h	42.8	51.7	0.0085

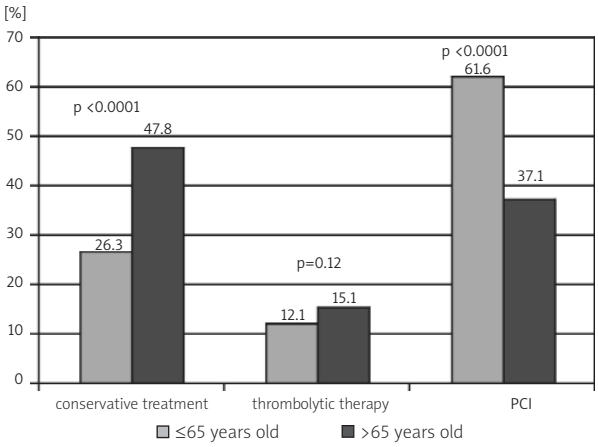

Figure 1. Strategy of myocardial infarction therapy in two age groups: ≤65 years old and >65 years old

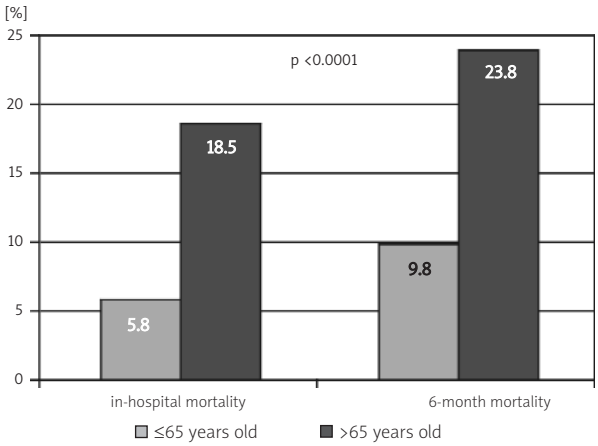

Figure 2. Comparison of in-hospital and long--term mortality between two age groups: ≤65 years and >65 years old

Myocardial infarction was significantly more often associated with intraventricular conduction disturbances (especially left bundle branch block) in older patients. An analysis of time to hospitalisation delay showed a significantly higher percentage of patients aged >65 years being hospitalised after four hours from the onset of infarction pain, as compared to the younger group (Table II).

Compared with the younger age group, older patients less frequently received reperfusion therapy. Older people aged >65 were significantly less frequently qualified for coronary interventions. Despite comparably frequent thrombolytic therapy in both populations, older patients had conservative treatment significantly more often than younger patients (Figure 1).

In older patients direct effects of revascularisation were significantly worse than those achieved in the younger age group. Final flow in the infarct-related artery assessed according to TIMI scale was TIMI 3 in 90.7% of patients aged >65 compared to 95.5% aged ≤65 (p <0.045).

The analysis of pharmacological treatment in two age categories showed that aspirin (92.9 vs. 96.2%, p= 0.031), antiplatelet agents – clopidogrel (39.9 vs. 65.6%, p <0.0001) and GP IIb/IIIa inhibitor (11.6 vs. 23.9%, p <0.0001), and heparin (35.2 vs. 52.8%, p <0.0001) were significantly less frequently used in the older group. Of note, beta-blockers, statins and converting enzyme inhibitors were similarly often included in therapy of both older and younger patients.

In-hospital and long-term mortality of older subjects were high and remained significantly higher in comparison with mortality in the younger age group (Figure 2). The best short-term and long-term prognosis turned out to be in older patients treated using invasive strategy: 6-month mortality in the elderly group dropped by 62% as opposed to patients of the same age receiving medical therapy only. Significant survival improvement in patients >65 years old was observed after administration

of thrombolysis (34% mortality reduction at 6-month follow-up). In-hospital and long-term mortality were by far the highest in older patients treated conservatively (Figure 3).

The probability of being alive at 6 months was 0.77 for subjects >65 years old and 0.90 for patients aged ≤65 years (Figure 4).

Discussion

Clinical course of acute coronary syndromes (ACS) in older subjects often shows differences when compared with the younger population. Older people less frequently than young ones experience typical chest pain, but more often complain of dyspnoea, abdominal pain or fatigue, which is frequently falsely assumed to represent the natural consequence of aging or the progression of elderly-related conditions [8].

Frequent, atypical, silent course of MI in the older group is interpreted as a consequence of elevated pain threshold in this group, even without concomitant diabetes. On the other hand, elevated pain threshold probably stems from damaged sensory fibres caused by chronic myocardial ischaemia, disturbances of cerebral cortex function dependent on cerebral ischaemia or autonomic dysfunction [9].

Due to atypical MI symptoms, impaired mobility and lack of means of transportation, older patients with ACS presented to the medical facilities later than younger ones. According to one of the analyses regarding causes of the delayed initiation of MI treatment, 30% of patients aged >65 years reach hospital more than 6 hours after the onset of symptoms [10].

This study also showed more frequent delay of time to hospital admission in older as opposed to younger ones – 50% of patients aged >65 years presented to hospital more than 4 hours from the onset of chest pain. It is undoubtedly not the only reason for higher MI mortality in older people. What should also be taken into account is the age-related growing number of risk factors together with worse baseline clinical characteristics of older patients – lower LVEF with more frequent symptomatic heart failure. A great problem is the apparently less frequent referral of older people for reperfusion.

According to available data, invasive revascularisation of coronary arteries has not often been used in older people since its introduction to MI therapy standards. Analysis of a large database from 1992-1993 indicated that percutaneous coronary intervention (PCI) was performed in 17% of patients in the group >75 years of age, whereas in patients aged 65-74 years PCI was done in 43% of MI patients [11]. Currently, in the USA 20% of PCI and CABG procedures are performed in patients aged >75 years and >50% of procedures involve patients aged >65 years. [3]. Certainly, qualification of older people for invasive treatment each time requires individual risk and benefits assessment. According to some reports, it is less likely to restore perfusion in the infarction area in older people than in younger ones, which significantly contributes to higher mortality. This was confirmed in the analysis of perfusion using the Myocardial Blush Grade (MBG) scale along with evaluation of ST segment resolution in approximately 1,500 patients treated with primary PCI due to ST segment elevation MI (STEMI). This observation confirmed the linear correlation between increasing age, worsening myocardial perfusion and lower ST segment resolution in ECG and together with these factors increasing one-year mortality [12].

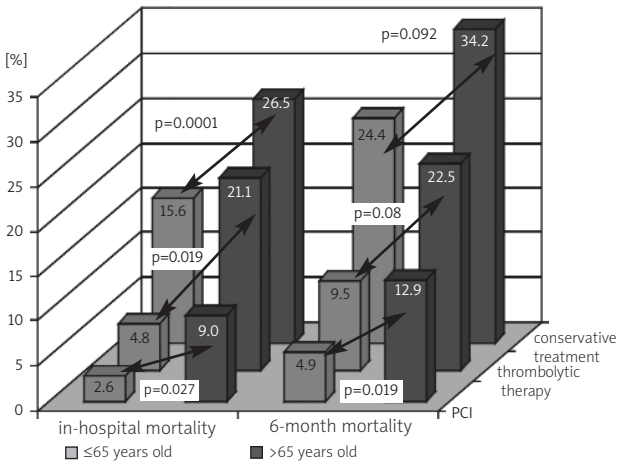

Figure 3. Comparison of in-hospital and long-term mortality between both age groups with respect to the treatment strategy used

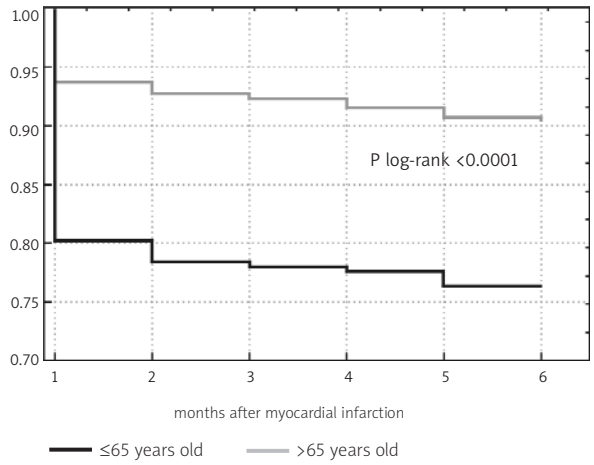

Figure 4. Kaplan-Meier survival curves over 6-month follow-up in patients aged ≤65 and >65 years. Patients hospitalised due to myocardial infarction from June 2005 to February 2006

According to other reports having progressively better interventional techniques, similar effectiveness was gained in restoring potency of the culprit artery and restoring perfusion in older people (>75 years old) in comparison with the younger age group. Despite that fact, older age mortality rate reached 15% at 30 days and 21% at 1 year post PCI procedure, whereas in the group of younger patients (mean age of 59 years) mortality rate reached 1% at 30 days and 3% at one year [13].

Our study revealed significantly worse efficiency of interventions in patients >65 years old compared to younger ones. In addition, in-hospital and long-term mortality were much higher in older patients who underwent invasive therapy than in those younger patients treated with PCI.

Using a large-scale register of ACS (>8,000 patients with STEMI hospitalised in 2000-2002) the method of treatment and long-term prognosis in 2045 patients aged >75 years were analysed. It turned out that 51% of patients underwent conservative treatment, 19% received thrombolytic therapy while in 30% primary PCI (pPCI) was performed. In-hospital mortality was as follows: 23.4% in the conservative treatment group, 25.4% with the use of fibrinolytics and 10.2% in the PCI group; thus at one year the total mortality was 52.4% in patients treated conservatively, 41.3% following thrombolysis and 19.3% following invasive therapy. Of course this observation showed high MI-related mortality in older patients. Nevertheless, there were undeniable benefits from the use of pPCI; besides, the multivariate analysis in this patient group showed good long-term results of thrombolysis despite high in--hospital mortality [14].

Other contemporary observations emphasise that using more aggressive MI therapy in older subjects is associated with better long-term outcomes. In the study involving a small population of 102 patients aged >75 years who were hospitalised due to STEMI, 50 patients were treated with primary PCI while the remaining 52 subjects were qualified for conservative treatment. Both groups were similar with respect to sex distribution, coronary artery disease risk factors, localisation of MI and clinical status on admission. In comparison with patients treated conservatively, during the course of hospitalisation subjects after pPCI experienced significantly less frequent recurrent ischaemia. Although the frequency of combined endpoint was similar in both groups of patients during in-hospital and 30-day follow--up, after one year the rates of adverse events and mortality in patients undergoing PCI were reported as significantly lower [15].

At present, despite relatively few studies confirming the beneficial influence of reperfusion therapy in older people, it is believed that age as such is not a contraindication to reperfusion in MI. As a matter of fact, the choice of this therapy should be individualised, weighing both potential risks and benefits.

Another problem in the treatment of ACS in older people remains the use of pharmacological treatment as recommended by the guidelines. It is often thought that for patients at older age advantage of the entire range of possibilities offered by contemporary cardiology is not taken. According to data published in the USA in 1996 regarding pharmacotherapy in acute MI, in older people thrombolysis was applied less frequently than in younger ones; in addition, they also received aspirin and beta-blockers less often than younger patients [16]. A similar study was conducted in our institution in 1992-1996, confirming observations that the use of fibrinolytic drugs, aspirin, beta-blockers and anticoagulants in older groups was significantly reduced [17]. Beneficial effects of these agents in the treatment of ACS have been clearly documented in all age groups, and so they should be used in older patients as well.

Benefits from administration of aspirin in acute MI were demonstrated in the ISIS-2 study. Subsequent analyses of the study also confirmed positive effects of the drugs in patients aged over 70 years [18]. Aspirin use as secondary prevention in older people has been validated as well – 19% reduction of mortality risk, re-infarction and stroke in patients >65 years of age, which means even greater absolute risk reduction in this patient category as compared with younger ones [19]. Aspirin and new antiplatelet drugs have been shown in our study to be used significantly less frequently in patients >65 years old.

Current analysis of in-hospital and long-term mortality in patients aged >65 years as opposed to younger ones confirmed a close correlation between the impact of modern treatment methods and the prognosis of this patient group. In spite of constantly worse invasive treatment results in older people, the benefits of its use are huge in this population.

In summary, in view of the constantly growing population of older people in most societies, the percentage of patients treated due to MI at older age is rising as well. Due to different clinical course and too careful approach to invasive and pharmacological therapy, high in-hospital and long-term mortality are still being observed in this patient group.

Conclusions

1. Due to the aging of society, MI incidence at older age is a growing therapeutic challenge.

2. Differences in clinical course, worse baseline clinical characteristics and often poor socio-economic status that have to be faced in the case of older patients contribute to poor prognosis in this patient group.

3. The not fully justified fear of medical staff often results in disqualification of older patients from reperfusion

therapy and usually from concomitantly taken modern antiplatelet therapy. However, a greater improvement of short- and long-term prognosis was shown in patients aged >65 years treated especially with pPCI.

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Zawał serca u osób w starszym wieku. Odrębności kliniczne i różnice w terapii

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Streszczenie

Wstęp: Postępujący proces starzenia się społeczeństwa wpływa na wzrost populacji chorych, u których zawał serca (MI) dokonuje się w podeszłym wieku. Wobec olbrzymiego postępu leczenia MI na przełomie XX i XXI wieku, istotna wydaje się odrębna analiza przebiegu klinicznego i rokowania u osób starszych.

Cel: Ocena odrębności klinicznych i postępu terapii MI u chorych z województwa świętokrzyskiego, hospitalizowanych z powodu ostrego zespołu wieńcowego z uniesieniem odcinka ST (STEMI) w okresie od czerwca 2005 do lutego 2006 r.

Metodyka: Retrospektywna analiza porównawcza przebiegu klinicznego oraz rokowania odległego u 491 chorych w starszym wieku (>65. roku życia) oraz 398 osób młodszych (≤65. roku życia) hospitalizowanych z powodu STEMI w Świętokrzyskim Centrum Kardiologii w okresie od czerwca 2005 do lutego 2006 r.

Wyniki: U chorych w wieku >65 lat hospitalizowanych z powodu ostrego STEMI stwierdzono istotnie częstsze występowanie nadciśnienia tętniczego i cukrzycy w porównaniu z młodszą grupą wiekową. U chorych starszych wykazano również gorsze parametry frakcji wyrzutowej lewej komory i wyższy stopień zaawansowania niewydolności krążenia ocenianej wg klasyfikacji Killipa-Kimballa. Chorzy >65. roku życia byli znamiennie później hospitalizowani z powodu MI w porównaniu z osobami młodszymi. Starsi chorzy, w porównaniu z młodszą grupą wiekową, rzadziej otrzymywali leczenie reperfuzyjne w ostrej fazie MI (52,2 *vs* 73,7%), przy czym bezpośrednie efekty zabiegów rewaskularyzacyjnych u osób starszych były istotnie gorsze. Stwierdzono ponadto stosowanie mniej intensywnej terapii lekami przeciwpłytkowymi u chorych >65. roku życia. Śmiertelność wewnątrzszpitalna i odległa była istotnie wyższa w starszej niż w młodszej grupie wiekowej (odpowiednio: 18,5 *vs* 5,8%, p <0,0001 oraz 23,8 *vs* 9,8%, p <0,0001), przy najniższej liczbie zgonów wśród chorych leczonych inwazyjnie.

Wnioski: Gorsza charakterystyka kliniczna oraz zbyt rzadkie stosowanie leczenia reperfuzyjnego u osób >65. roku życia przyczyniają się do gorszego rokowania w tej grupie chorych. Wykazana znacząca redukcja śmiertelności u starszych chorych leczonych inwazyjnie powinna zachęcać do szerszego wdrażania intensywnego leczenia MI w tej grupie wiekowej.

Słowa kluczowe: zawał serca, starszy wiek, terapia reperfuzyjna

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