Primary coronary intervention in diabetic octogenarians with acute ST elevation myocardial infarction

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Abstract

Background: Diabetic patients with acute coronary syndrome (ACS) have higher mortality risk than non-diabetic patients. No data are available on long-term results of interventional treatment of ACS in diabetic patients aged ≥80 years.

Aim: To compare the effects of primary angioplasty (pPCI) on short- and long-term outcome in diabetic patients ≥80 years with ST-elevation myocardial infarction (STEMI) compared to those without diabetes mellitus (DM) of similar age.

Methods: In 63 consecutive patients (22% with diabetes mellitus) aged 80-93 years (mean 83±3) with ST elevation ACS (ACS-STE) coronary angiography was performed. Severity of coronary atherosclerosis, effects of pPCI, one-day mortality, in-hospital mortality and one-year mortality were studied.

Results: Severity of coronary atherosclerosis measured by angiographic Gensini score and author’s own score was similar in diabetic and non-diabetic patients (23.25±9.6 vs. 20.6±10.2; NS, and 9.1±6.0 vs. 8.1±5.4; NS, respectively). In 78.6% of diabetic subjects and in 69.4% of those without DM, pPCI was performed. Successful pPCI, defined as TIMI 3 flow and residual infarct related stenosis <20%, was obtained in 92.2% of patients with DM compared to 83.7% of non-diabetics (OR=0.31; p <0.05). Contrast-induced nephropathy occurred in 35.7% of diabetic patients compared to 26.5% of those without diabetes (NS). Contrast-induced nephropathy increased risk for in-hospital mortality fivefold (p <0.02). No significant correlation between DM or baseline glucose level and in-hospital mortality was found. During one-year follow-up mortality rate in diabetic patients was 38.5% compared to 7.3% of those without diabetes (p <0.01). One-year mortality predictors were: age (OR=1.27; p=0.0047), metabolic syndrome (OR=4.4; p <0.04), type 2 diabetes (OR=5.23; p <0.02), insulin treatment (OR=5.7; p <0.03), baseline glucose level (OR=1.01; p <0.007), maximum CK-mass level (OR=1.006; p <0.05), noninvasive STEMI management (OR=5.0; p <0.02), and stroke (OR=7.5; p <0.006). Stroke (OR=40.0; p <0.005) and diabetes (OR=6.2; p <0.01) were identified by multivariable analysis as independent risk factors of one-year mortality.

Conclusions: In patients with DM aged ≥80 years with ACS-STE, severity of coronary atherosclerosis and in-hospital prognosis after pPCI seems to be similar to subjects in the same age without DM. Diabetes mellitus is an independent risk factor of one-year mortality after successful pPCI.

Key words: acute coronary syndrome, primary coronary intervention, diabetes mellitus, elderly

Introduction

In Poland, as in many Western countries, the percentage of elderly people in the human population continues to increase due to longer average life span and decreased birth rates. Prevalence and mortality due to cardiovascular diseases and other chronic disorders, including diabetes mellitus (DM), increase with aging. More than 50% of patients with type 2 DM die of coronary artery disease [1, 2]. The current potential of modern medicine, including invasive cardiology, is not fully employed in the treatment of elderly patients, particularly...
those with coexisting diabetes [3, 4]. Studies indicate that patients hospitalised for acute coronary syndromes with ST elevation (ACS-STE) with concomitant DM are at higher risk of cardiogenic shock, recurrence of myocardial ischaemia despite successful revascularisation, death and other complications than non-diabetic patients [3, 4]. However, current standards of ACS-STE management are based on the evidence from randomised trials involving patients mean aged 60 to 64 years, and the range of standard deviations indicates that representation of patients aged 80 years or more is very limited [5]. Also, little is known about the efficacy and safety of primary percutaneous coronary intervention (pPCI) in patients aged ≥80 years. Moreover, evaluation of the impact of DM on the early and long-term results of pPCI in this group of patients has not been investigated so far.

The purpose of this study was to evaluate the severity of coronary artery atherosclerotic lesions and the applicability, efficiency and safety of pPCI in patients presenting with both type 2 DM and ACS-STE aged ≥80 years.

Methods

Patients

The study involved 63 consecutive patients with ACS-STE aged 80 to 93 years (mean 82.9±3.2 years), including 14.3% with cardiogenic shock. This group was selected out of a cohort of 438 consecutive patients who underwent coronary angiography due to ACS-STE. Coronary angiography was performed in all patients. Analysis involved the assessment of coronary atherosclerosis burden by means of modified angiographic Gensini score [6] and the author’s original angiographic index $a (a = b \times 1 + c \times 2 + d \times 3 - e \times 1$, where $a$ stands for index of coronary atherosclerosis burden, $b$ is the number of segments with significant isolated lesions, $c$ is the number of arterial segments with diffuse atherosclerosis, $d$ is the number of completely occluded segments, and $e$ is the number of segments perfused from the collateral coronary circulation). First, feasibility of pPCI was analysed (it was a single subjective assessment done by the operators and based on their own experience; each of them performed at least 500 pPCI procedures), then pPCI was carried out if indicated. In the case of giving up the pPCI attempt or PCI failure, patients were treated conservatively.

Patients with type 2 DM accounted for 22.2% of the examined group (n=14). Diabetes mellitus was defined as disease previously diagnosed and documented in the medical records or as de novo disease according to Polish Diabetological Society 2004 guidelines criteria. Study group characteristics with respect to type 2 DM coexistence are shown in Table I.

PCI procedures

PCI procedure was preceded by unfractionated heparin administration (at least 5000 U) to reach the target ACT ≥300 seconds and after oral 500 mg aspirin dose (if on chronic aspirin before PCI, no extra dose was given) and clopidogrel loading dose of 300 mg given not later than immediately prior to patient transfer to the cath lab. After blood flow in the infarct-related artery was restored, an intravascular bare-metal stent (BMS) was implanted at the

Table I. Study group baseline characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diabetes mellitus (-)</th>
<th>Diabetes mellitus (+)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men [%]</td>
<td>32.6</td>
<td>28.6</td>
<td>NS</td>
</tr>
<tr>
<td>Age [years]</td>
<td>83.0±3.2</td>
<td>84.2±2.9</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension [%]</td>
<td>71.4</td>
<td>85.7</td>
<td>NS</td>
</tr>
<tr>
<td>Metabolic syndrome [%]</td>
<td>4.1</td>
<td>64.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hyperlipidaemia [%]</td>
<td>18.8</td>
<td>42.9</td>
<td>0.05</td>
</tr>
<tr>
<td>History of myocardial infarction [%]</td>
<td>30.6</td>
<td>42.9</td>
<td>NS</td>
</tr>
<tr>
<td>Diagnosis of heart failure [%]</td>
<td>22.9</td>
<td>35.7</td>
<td>NS</td>
</tr>
<tr>
<td>Peripheral artery disease [%]</td>
<td>16.3</td>
<td>14.3</td>
<td>NS</td>
</tr>
<tr>
<td>Previous stroke/transient ischaemic attack [%]</td>
<td>4.2</td>
<td>7.1</td>
<td>NS</td>
</tr>
<tr>
<td>Renal failure [%]</td>
<td>16.3</td>
<td>28.6</td>
<td>NS</td>
</tr>
<tr>
<td>History of percutaneous coronary intervention [%]</td>
<td>6.1</td>
<td>14.3</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiogenic shock [%]</td>
<td>14.3</td>
<td>14.3</td>
<td>NS</td>
</tr>
<tr>
<td>Glucose level on admission [mg/dl]</td>
<td>150.7±43.0</td>
<td>212.1±62.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Creatinine concentration on admission [mg/dl]</td>
<td>1.19±0.41</td>
<td>1.37±0.55</td>
<td>NS</td>
</tr>
<tr>
<td>Blood urea nitrogen concentration on admission [mg/dl]</td>
<td>50.7±23.7</td>
<td>65.9±16.4</td>
<td>NS</td>
</tr>
<tr>
<td>Time from symptom onset to coronary angiography [h]</td>
<td>3.6±3.2</td>
<td>3.6±3.3</td>
<td>NS</td>
</tr>
</tbody>
</table>
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site of the ruptured atherosclerotic plaque. Primary coronary angioplasty was defined as successful if restored blood flow was TIMI 3 in the ACS-related coronary artery and residual stenosis following stent deployment was <20%.

End-points

In-hospital, 30-day and one-year mortality as well as complications associated with intervention such as death (within 24 hours from hospital admission), rate of contrast-induced nephropathy and bleeding events were assessed.

Statistical analysis

Statistical analysis was based on $\chi^2$ and Fisher’s test for qualitative variables and on Student’s t-test when quantitative variables were compared. Results of the tests were considered statistically significant if a $p$ value was <0.05. Quantitative variables were expressed as mean ± standard deviation. Survival analysis and identification of mortality risk factors were performed based on proportional distribution of Cox risk model (PHREC procedure) and multivariate logistic regression analysis. All calculations were carried out using the SAS statistical software.

Results

Severity of coronary atherosclerosis assessed by modified Gensini score and author’s own formula did not differ between DM(+) and DM(−) groups (Figure 1). In 78.6% of diabetic and in 69.4% of non-diabetic patients a pPCI attempt was made (NS), and its efficacy measured as coronary flow restoration achieving TIMI 3 was 92.9% and 83.7%, respectively (NS). Acute coronary angioplasty of at least two arteries as a therapy for ASC was carried out in 0 and 14.3% (p <0.02) of these patients, while during the entire hospitalisation period complete percutaneous myocardial revascularisation was performed in 21.4 and 34.7% of patients, respectively (NS). In 14.3% of diabetic and in 24.5% of non-diabetic patients GP IIb/IIIa inhibitors, most often abciximab, were used (p=0.02). The infarct-related artery characteristics, pPCI efficiency rate and selected parameters describing treatment results are outlined in Table II. Periprocedural mortality was 7.1% in the group of diabetic patients and 6.1% in the non-diabetics patients (NS), while in-hospital mortality was 7.1 and 16.3%, respectively (NS).

Table II. Angiographic and in-hospital results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diabetes mellitus (−) n=49</th>
<th>Diabetes mellitus (+) n=14</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarct-related artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left interior descending/diagonal branch [%]</td>
<td>61.2</td>
<td>57.2</td>
<td>NS</td>
</tr>
<tr>
<td>Circumflex/marginal branch [%]</td>
<td>4.1</td>
<td>7.1</td>
<td>NS</td>
</tr>
<tr>
<td>Right coronary artery [%]</td>
<td>34.7</td>
<td>35.7</td>
<td>NS</td>
</tr>
<tr>
<td>‘No-reflow’ phenomenon [%]</td>
<td>2.0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Peak CK-mass (mean±SD) [U]</td>
<td>87.4±110.6</td>
<td>101.1±123.7</td>
<td>NS</td>
</tr>
<tr>
<td>Local haemorrhagic complications [%]</td>
<td>22.4</td>
<td>7.1</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding requiring blood transfusions [%]</td>
<td>18.4</td>
<td>7.1</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding to CNS [%]</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Contrast-induced nephropathy [%]</td>
<td>26.5</td>
<td>35.7</td>
<td>NS</td>
</tr>
<tr>
<td>Subacute in-stent thrombosis [%]</td>
<td>2.0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Left ventricular ejection fraction at discharge (mean±SD) [%]</td>
<td>44.6±12.4</td>
<td>37.8±14.2</td>
<td>NS</td>
</tr>
<tr>
<td>Heart failure at discharge [%]</td>
<td>22.9</td>
<td>35.7</td>
<td>NS</td>
</tr>
<tr>
<td>Hospitalisation time (mean±SD) [days]</td>
<td>16.7±9.4</td>
<td>16.4±12.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

Figure 1. Comparison of the severity of coronary artery atherosclerosis expressed as angiographic Gensini score and author’s own formula between diabetic (black bars) and non-diabetic (gray bars) patients

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Among patients discharged from the hospital, 61.5% of diabetic and 92.7% of non-diabetic patients survived at least one year (p <0.01). Annual survival rate in the whole group of patients with or without DM is shown in Figure 2. Significant identified risk factors for death are presented in Figure 3. Logistic regression analysis identified DM and previous stroke as the independent risk factors of cardiovascular mortality during one-year follow-up (OR=6.2; p <0.01 and OR=40.0; p <0.005, respectively).

**Discussion**

Optimal therapeutic strategy in patients with coronary artery disease and DM aged ≥80 years has not yet been described. The presence of advanced stage of atherosclerosis makes it difficult to make decisions regarding referral to coronary interventions. Coexistence of DM theoretically increases the likelihood of treatment failure, as studies on atherosclerosis, conducted on younger patients, showed that in diabetic patients atherosclerosis develops earlier and its progression is much more rapid when compared to non-diabetics patients. Diabetes mellitus results in more severe coronary artery atherosclerosis; degenerative lesions are often more complex and diffused, involving peripheral coronary segments [7-9]. Thus, early and long-term clinical outcomes of coronary interventions in patients with such changes seem to be less favourable [3, 4]. Keeping that in mind, physicians treating patients aged ≥80 years relatively often decide not to perform coronary angiography or pPCI.

The results presented in this study seem to contradict this way of thinking because the severity of coronary artery disease in patients with type 2 DM aged ≥80 years did not differ significantly from control patients without diabetes. Similarly, clinical presentation on admission was comparable in diabetic and non-diabetic subjects. Baseline differences were suggested by the results of studies that involved younger patients [3, 10]. Moreover, in our patients the rates of successful reperfusion, early in-stent thrombosis and in-hospital mortality were similar in the DM(+) and DM(−) patients and this fact should in the future prompt the qualification of patients presenting similar symptoms for interventional procedures.

The results presented in this report are in the opposition to the usual approach to the elderly with DM by an interventional cardiologists which is based on the assumption that it is difficult or even impossible to perform successful pPCI in this group of patients. Because of the extent and severity of atherosclerotic changes, operators did not attempt to restore blood flow in the coronary infarct-related artery in approximately 25% of patients. However, these patients, even after medical stabilisation, were at the high risk of one-year mortality associated with end-stage of coronary artery atherosclerotic disease rather than no attempt at revascularisation itself. Taking into consideration the inapplicability of fibrinolysis (due to patient’s age) and the fact that in more than 75% of the examined patient group reperfusion of the infarct-related artery was achieved, we believe that our results support attempting interventional therapy in the ACS-STE patients aged ≥80 years.

Early efficacy and safety of pPCI in the examined group seems to be, at least partially, in opposition to the studies reporting an unfavourable impact of DM on early results of ACS interventional treatment as TIMI 3 flow was restored in a similar percentage of patients with and without DM. However, attention must be paid to the statistically insignificant, but more than 9% higher, pPCI efficiency in diabetic patients. We believe that the relatively small number of patients in the study groups may account for this finding. Moreover, suspicion of a higher prevalence of the ‘no-reflow’ phenomenon in diabetic patients was not confirmed [11]. Analysis of the results revealed relatively frequent use of intravenous GP IIb/IIIa inhibitors in this group (age of ≥65 years is a relative contraindication to the use of abciximab), and less frequent use in diabetic patients representing a group of patients in whom such a therapy is
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particular beneficial [12, 13]. Such aggressive antiplatelet therapy was found to be relatively safe and no life-threatening hemorrhagic complications were noted. The relatively rare local complications in DM patients in comparison to the non-DM group are surprising. This may be associated with more common triple antiplatelet therapy in the non-diabetic patient group. Moreover, recognition of higher risk of complications in diabetics prompted earlier arterial sheath removal or more meticulous haemostasis.

Diabetes mellitus and age of ≥75 years are widely accepted risk factors for development of contrast-induced nephropathy [14]. The rate of nephropathy in the group of patients analysed herein was alarming, and an additional unfavourable effects of diabetes were seen, although not reaching statistical significance.

Our observations confirm the findings of many earlier studies reporting a negative impact of DM [13, 15, 16] and hyperglycaemia [16, 17] on long-term prognosis in patients after MI despite successful pPCI. The detailed mechanism of this phenomenon has not been identified. However, it is known that besides more frequent clinically silent restenosis in this patient group [18], hyperglycaemia increases myocardial necrosis area due to the abnormal stimulation of immunologic inflammatory processes. A significant correlation between increased serum glucose concentration and inflammation markers such as CRP and IL-18 peripheral blood level, increased cytotoxic T cell activity and suppressed expression of T cells involved in alleviation of immunologic processes has been shown [19].

The main limitation of the present study is the relatively small number of patients in the groups, especially diabetics. Thus, interpretation of our results should be done with particular caution. The presented patient group represents only a part of a single-centre annual registry. Thus, continuation of follow-up and repeat analysis involving more patients has been planned.

Conclusions

In type 2 diabetic patients aged ≥80 years with ACS-STE, severity of coronary artery atherosclerosis, feasibility of coronary intervention and early pPCI efficacy seem to be similar to non-diabetic patients. However, DM and glucose level on admission are the independent risk factors of death during one-year follow-up, despite successful pPCI procedure.

References

Pierwotna angioplastyka wieńcowa u chorych na cukrzycę typu 2 z ostrym zespołem wieńcowym z przetrawałym uniesieniem odcinka ST w wieku od 80 lat

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Streszczenie

Wstęp: Wyniki badań wskazują, że chory na cukrzycę typu 2 z ostrym zespołem wieńcowym (ACS) z towarzyszącą cukrzycą mają wyższe ryzyko wstrząsu kardiogennego, nawrotu niedokrwienia pomimo skutecznej reperfuzji, zgonu oraz innych powikłań w porównaniu z chorymi bez cukrzycy. Metodą z wyboru leczenia ACS z przetrawałym uniesieniem odcinka ST (ACS-STE) jest pierwotna przezskórna angioplastyka wieńcowa (pPCI). Współczesne standardy postępowania w ACS powstały jednak na podstawie wyników badań z randomizacją, przeprowadzonych w grupie chorych w średnim wieku <75 lat. Dotychczas nie badano wpływu cukrzycy na wyniki leczenia pPCI chorych z ACS-STE w wieku ≥80 lat.

Cel: Ocena zaawansowania miażdżycy tętnic wieńcowych, przydatności i wyników pPCI u chorych na cukrzycę z ACS-STE w wieku ≥80 lat.

Metoda: Badaniem objęto 63 chorych (22,2% z cukrzycą typu 2) w wieku 80–93 lat (średnia 83±3), u których w przebiegu ACS-STE wykonano koronarografię. Oceniono zaawansowanie miażdżycy tętnic wieńcowych, obliczając zmodyfikowany wskaźnik Gensiniego i autorski wskaźnik angiograficzny

\[ a = b \times 1 + c \times 2 + d \times 3 - e \times 1; \]

где: 
- \( a \) – wskaźnik zaawansowania zmian miażdżycowych, 
- \( b \) – liczba segmentów z istotnymi izolowanymi zwężeniami, 
- \( c \) – liczba segmentów tętnic z rozsianymi zmianami miażdżycowymi, 
- \( d \) – liczba segmentów niewypełniających się (niedrożnych), 
- \( e \) – liczba segmentów dobrze wypełniających się z krążenia obocznego. Ponadto przeanalizowano możliwości i bezpieczeństwo wykonania pPCI, śmiertelność w pierwszej dobie i wewnątrzszpitalną oraz przeżycie roczne.

 Wyniki: Zaawansowanie miażdżycy w tętnicach wieńcowych, ocenione angiograficznym współczynnikiem Gensiniego oraz wzorem autorskim, u chorych na cukrzycę i u chorych bez cukrzycy było podobne (odpowiednio: 23,25±9,6 i 20,6±10,2; NS oraz 9,1±6,0 i 8,1±5,4; NS). U 78,6% chorych na cukrzycę i u 69,4% osób bez cukrzycy podjęto próbę pPCI (NS). Jej skuteczność mierzona przywróceniem przepływu wieńcowego TIMI 3 i zwężeniem rezydualnym <20% wynosiła odpowiednio 92,9 i 83,7% (NS), śmiertelność okołoizolowana (w ciągu 24 godz. od pPCI) 7,7 i 6,1% (NS), a całkowita śmiertelność w ciągu doby 0,9% (NS). Analiza statystyczna nie wykazała związku pomiędzy cukrzycą a zgonem wewnątrzszpitalnym. Wśród chorych, którzy przeżyli okres hospitalizacji, śmiertelność chorych na cukrzycę w czasie obserwacji rocznej wyniosła 38,5%, a chorych bez cukrzycy 7,3% (p <0,01). Logistyczna analiza regresji wykazała, że cukrzycy i przebyty udar mózgu były niezależnymi czynnikami ryzyka zgonu z przyczyn sercowo-naczyniowych w ciągu roku obserwacji (odpowiednio OR=6,2, p <0,01 i OR=40,0, p <0,005).

Wnioski: U chorych na cukrzycę typu 2 w wieku ≥80 lat z ACS zaawansowanie zmian miażdżycowych w tętnicach wieńcowych, możliwość wykonania i skuteczność doraźnej pPCI wydają się podobne do stwierdzonych u chorych bez cukrzycy. Cukrzyca jest jedynie czynnikiem ryzyka zgonu w ciągu roku obserwacji, pomimo skutecznej pPCI.

Słowa kluczowe: ostry zespół wieńcowy, pierwotna angioplastyka wieńcowa, cukrzyca typu 2, wiek

Kardiol Pol 2007; 65: 1181–1186

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