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INFLUENCE OF DIABETES MELLITUS ON SHORT TERM MORTALITY IN PATIENTS WITH FIRST ACUTE ST - ELEVATION MYOCARDIAL INFARCTION: A TEN YEARS RETROSPECTIVE STUDY

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ABSTRACT. The objective was to compare short-term mortality after a first acute myocardial infarction with ST elevation (STEMI) in patients with and without diabetes mellitus (DM). Between 1.01.2000 - 31.12.2009, 1335 STEMI patients were admitted in the Baia Mare Emergency Hospital: 660 (142 DM) had no thrombolysis, 675 (136 DM) received thrombolysis. In-hospital mortality was 19.4% in the 278 DM patients and 14.3% in the 1057 non-DM patients (p=0.002). Mortality in the subgroups was different: 11.3% in the 539-thrombolysed non-DM patients, 16.5 % in the 136-DM thrombolysed patients (p=0.01) and 21.4% in 142 DM patients without thrombolysis (p<0.0001). DM patients had more failed thrombolysis, 5.8% vs. 2.1%, and more recurrent ischemia, 9.3 % vs. 4.6 %, than non-DM patients had (p=0.002). Short-term mortality after a first STEMI in DM patients is higher due to a worse clinical profile but also to a less effective myocardial reperfusion.

Keywords: mortality, STEMI, diabetes mellitus, thrombolysis, myocardial reperfusion

INTRODUCTION

"54 –years, old obese male suffering from hypertension with a prior history of diabetes mellitus (DM) arrives at emergency room diagnosed with anterior ST elevation (STEMI) acute myocardial infarction. Physical and radiological tests show evidence of left ventricular dysfunction, the admission glycemic index is 245 mg/dl. Coronarography shows evidence of anterior descending coronary artery occlusion and the subsequent stent implantation angioplasty restores TIMI-3 flow. Angiographic ejection fraction (EF) is 38% while the kinetic parameters of each segment are highly modified by severe extended hypokinesias. Acute enzyme increase does not exceed 650 UI/L for creatin kinase (CPK) while the next day glycemic index is 185 mg/ dl. On leaving the hospital, the glycemic index is 146 mg/dl and after 8 weeks' follow up, echocardiography shows evidence of EF = 35% quantified by volume, with no improvement of segmental kinetics.

Afore described clinical scenario is quite common and it highlights the way in which DM, favored by a subnormal coronary perfusion (after a successful angioplasty) and an incomplete myocardial healing (even if the enzyme increase was reduced), can influence the evolution and prognosis of patients with STEMI.

DM is one of the main factors with negative influence upon the mortality rate in patients who develop acute myocardial infarction (AMI) [Capes et al., 2000; Cao et al., 2005]. The prevalence of DM among patients with acute coronary syndrome is 20 – 26%, but acute hyperglycemia is significantly more frequent, occurring in over 50% of those patients, even if they have no prior history of diabetes (Wahab et al., 2002)

The prevalence of Type 2 DM or a reduced glucose tolerance is close to 65% if testing with oral glucose loading is performed on a regular basis in patients who develop AMI (Kosiborod et al., 2005). In these patients admission glycemic levels as well as HbA1c

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glycosylated hemoglobin levels have been validated as independent in-hospital and even long- term mortality predictors (Malmberg et al., 1999; Capes et al., 2000). In the GRACE global registry, one of the most extended studies involving DM patients who have developed STEMI, high values of cardiovascular mortality rate have been correlated with a high-risk clinical profile and a suboptimal use of modern reperfusion strategies (Kristen et al., 2004). In Romania, the interventional possibilities are limited and coronary reperfusion is mainly performed through fibrinolysis (Tatu-Chitoiu et al., 2009).

The aim of the present study was in the first place to assess and to compare short-term mortality rate in patients with and without DM, who develop STEMI, and undergo therapy in an emergency hospital where the exclusive method of reperfusion in order to reestablish coronary blood flow, is pharmacological. The identification of clinical and para clinical features which contribute to the aggravation of prognosis in patients with STEMI and DM was studied as well.

MATERIALS AND METHODS

Data acquisition

The study had a retrospective character and it mainly consisted of medical observation analyses upon a batch of patients with no special selection, who presented inaugural STEMI and who had been admitted to the Baia Mare - County Emergency Hospital's intensive coronary care unit between 01.01.2000 – 31.12.2009.

DM was defined based on medical history and upon the criteria's of WORLD HEALTH ORGANISATION from 1999, modified in 2006: 1. Day glycemia ≥200 mg% (11, 1 mMol/L), 2. Repetitive fasting glycemia ≥126 mg% (7 mMol/L) or 3. Modified 2 hours test with oral glucose loading ≥200 mg% (11, 1 mMol/L)

STEMI was defined based upon clinical electrocardiography, and classical enzyme activity criteria: 1. Persistent, intense pain (over 15-20 minutes) with retrosternal or epigastric localization, with or without radiation to the left shoulder and/or upper limb and /or neck and/or left interscapular vertebrae and which did not cease after the administration of nitroglycerine; 2. ST segment elevation ≥ 0.2 mV in V2–V3 and/or ≥ 0.1 mV in other derivations or new left bundle branch block; 3. The pathological increase of (CK / CK-MB) enzymes as markers for the presence of myocardial necrosis, have subsequently been introduced in the database as well as a reference field for troponin levels. In patients who underwent pharmacological reperfusion procedures three suggestive non-invasive criteria had been applied with a view to obtain reperfusion: 1. rapid cessation of thoracic pain; 2. an over 50% decrease of ST segment elevation, compared to the initial value +/- the appearance of arrhythmias, as markers of reperfusion (compulsory criteria) 180 minutes after the debut of fibrinolysis; 3. The rapid increase of CK / CK-MB levels or that of troponin, with a peak in the first 12 hours after the debut of reperfusion therapy.

Data centralization

The final central database achieved after the registration of all the data obtained until 31 December 2009 was thoroughly checked by two separate investigators, in order to avoid any possible incompatibility between the different fields. The same database was checked as a whole and corrected, regarding the quality of the data introduced.

Data processing

The registered data were processed using SPSS 15.0 for Windows (LEAD Technologies, Inc). Two investigators performed the analysis and interpretation of the data centralized by years in an independent and comparative way. The assessment of variable frequency was made exclusively for patients whose data had been validated. Patients who did not have data for a variable, were excluded: For example, those patients who did not have data for the administration of anticoagulant, antiplatelet, statins, beta-blocker and ACE inhibitor

therapy and had the "ND" (no data) note in the respective fields.

The results obtained were displayed as proportions with standard and mean deviations. In order to compare mean values the "t-test" was used while for that of proportions, the "chi" square test. The $p < 0.05$ value was considered as having statistical significance.

RESULTS AND DISCUSSIONS

The patients enrolled. A total number of 1335 patients were included in the study. Myocardial infarction topography was mentioned in a number of 1239 patients, (91.9%). Of these 698 (56.3%) had anterior myocardial infarction and 637 (43.7%) had acute non-anterior myocardial infarction (Table 1).

TABLE 1

Patients' age, coronary risk factors and sex distribution

Patients	DM	NON-DM	„p"
No patients N=1335 (%)	278 (20.8%)	1057 (79.2%)	-
Men N=894/1335 (66.9%)	110/278 (39.5%)	784/1057 (74.1%)	0.001
Women N=441 /1335 (33.1%)	168/278 (60.4 %)	273/1057 (25.8 %)	0.001
Age +/- SD (median, years) 64.0 +/- 11	65+/- 9	63+/-13	0.01
Anterior AMI N=698/1239 (56.3%)	138/259 (53.3%)	560/980 (57.1%)	NS
Non-Anterior AMI N=541/1239 (43.7%)	121/259 (46.7%)	420/980 (42.8%)	NS
AMI history N=76/1228 (6.1%)	28/274 (10.4%)	48/954 (5.1%)	0.05
Hypertension N=560/1228 (45.6%)	148/274 (54.02%)	412/954 (43.2%)	0.01
Dyslipidemia N=534 /1228 (43.5 %)	135/274 (49 %)	399/954 (41.8 %)	0.05
Obesity N=218/1228 (17.7%)	62/274 (22.6%)	156/954 (16.4%)	0.02
Cigarettes Smoking N=598/1228 (48.7%)	125/274 (45.9%)	473/954 (49.6%)	NS

Legend: DM-diabetes mellitus; No – number; SD-standard deviation; AMI-acute myocardial infarction

Time of myocardial infarction onset – hospital admission. The period between the onset of myocardial infarction symptoms and admission into emergency unit could be determined in 980 patients (73.5%). The onset of myocardial infarction was registered based on the onset data introduced in the hospital documents, according to the patients' and/or eye-witnesses' description. The overall mean period between the onset of angina symptoms and admission into a healthcare unit was of 235 minutes. However, this period should not be equaled to that between the onset of myocardial infarction and entry into an emergency healthcare unit, which certainly was considerably shorter.

A number of 451 patients (46%) were hospitalized within the first 3 hours after the onset of the infarction and 255 (25.9%) within a period of 3 - 6 hours. Consequently two third of the patients were hospitalized within the first 6 hours after the onset of the infarction, that is, within the optimum period to initiate coronary reperfusion therapy. Other 143 patients (14.6%) were hospitalized within a period of 6-12 hours after the onset of the

infarction and 60 (6.1%) within a period of 12 - 24 hours.

TABLE 2

Periods between the onset of myocardial infarction symptoms, admission and start of therapy

	Mean period	DM	NON-DM	„p"
No. patients N=1335 (%)	**-**	**278 (20.8%)**	**1057 (79.2%)**	**-**
Time				
Onset AMI-admission (min., median) N=980/1335 (73.48%)	**245 min**	**268min** N=210	**231min** N=770	**0.001**
Onset AMI-admission 0-179 min. N=451/980 (46 %)	-	N=43/210 (20.4%)	N=408/770 (53 %)	0.001
Onset AMI-admission 180-359 min. N=255/980 (25.9 %)	-	N=62/210 (29.5%)	N=193/770 (25.%)	0.08
Onset AMI-admission 360-719 min. N=143/980 (14.6%)	-	N=52/210 (24.7%)	N=91/770 (11.8%)	0.001
Onset AMI-admission 720-1439 min. N=60/980 (6.1%)	-	N=20/210 (9.5%)	N=40/770 (5.1%)	0.05
Onset AMI-admission > 24 hours N=71/980 (7.4%)	-	N=33/210 (15.7%)	N=38/770 (4.9%)	0.01
Time				
Admission- treatment start (min, median) N=1013/1335 (75.8%)	**32 min**	**33.5 min** N=230 (22.7%)	**31min** N=783 (77.3%)	**NS**
Admission- treatment start < 30 min. N=435/1013 (42.9%)	-	N=98/230 (42.6 %)	N=337/783 (43 %)	NS
Admission- treatment start: 30-59 min. N=415/1013 (41%)	-	N=91/230 (39.5 %)	N=324/783 (41.4%)	NS
Admission- treatment start >60 min. N=163 /1013 (16.1%)	-	N=41/230 (17.8 %)	N=122/783 (15.6 %)	NS

Legend: DM-diabetes mellitus; No – number; AMI-acute myocardial infarction

On the other hand, 71 patients (7.4%) were hospitalized 24 hours after the onset of symptoms. Of these, 7 (0.7%) were hospitalized 7 days after the onset of symptoms.

Significant differences could be noticed regarding the entry into an emergency healthcare unit between female and male patients, the latter arriving 18 minutes earlier than the former. In addition, DM patients were admitted significantly later, (23 minutes later) compared to the overall mean period (Table 2).

Time of hospital admission – debut of therapy. The moment of specific STEMI therapy initiation was considered when either thrombolytic or conventional therapy was initiated (usually the beginning of anticoagulant therapy). The period between hospital admission and STEMI therapy initiation was registered in 1013 patients. The overall mean period between hospitalizations and therapy was 32 minutes. Therapy was initiated in the first 32 minutes after admission in 435 patients (42.9%) and in the second half hour after admission in 415 patients (41%). Practically, therapy was started in 84% of the patients in the first 60 minutes after admission; a number of 324 (48%) of the 675 patients who underwent thrombolytic therapy were treated in the first 30 minutes after admission, the optimum time according to therapy guides.

Despite the tendency of DM patients to delay seeking medical help, there were no significant differences regarding the admission and the initiation of therapy between DM and non-DM patients (Table 2.)

Patients' age and sex distribution. The mean age of patients included in the present study was of 64.0+/- 11 years, with a median of 65. A number of 894 patients were male (66.9%) and a number of 441 (33.04%) were female. DM patients mean age was 2 years greater that of non-DM patients (65+/- 9 compared to 63+/-13 years, $p < 0.01$). Female patients' mean age exceeded that of male patients by 7 years (70+/- 10, compared to 63+/- 11 years, $p < 0.001$; Table 1).

Coronary risk factors. The incidence of coronary risk factors could be determined in 1228 patients which represents 92% of the study patients. Arterial hypertension was the most frequent coronary risk factor in DM patients (54.02%) with a prevalence that was significantly higher than the 45.9% value found in cigarette smoking patients ($p < 0.001$). These were followed by dyslipidemia (38.1%), obesity (22.6%), diabetes and a prior history of myocardial infarction (10.4 %). Analysis of demographic characteristics and that of risk factors was done separately for DM patients compared to non-DM patients and it highlighted the presence of more frequent co morbidity (patients with prior history of MI), of major cardiovascular risk factors (HTA, dyslipidemia, and obesity), advanced age and female predominance (Table 1.)

Killip class on admission. Killip class on admission was mentioned in 1292 patients (96.7%). Of these 788 (60.9%) were in Killip class I, 208 (16.09%) in Killip class II, 131 (10.1%) in Killip class III and 165 (12.7%) in Killip class IV. Regarding all forms of heart failure described, in DM patients the episodes occurred with a much higher frequency: 22, 3% compared to 9, 8% for Killip class III and 17, 8 % compared to 8, 5% for Killip class IV (Tabel 3).

Therapy. A group of 660 patients (49.4%) underwent conventional therapy and 675 (50.6%) received thrombolytic therapy. In the group of 278 DM patients 142 (51.07%) received conventional therapy while 136 (48.9%) received fibrinolytic therapy. In patients undergoing thrombolytic therapy, physicians progressively showed preference for fibrin specific thrombolytic therapy and 2007 was the first year when the number of patients receiving fibrin specific thrombolytic therapy exceeded that of patients receiving streptokinase therapy and the tendency became even more prominent in 2008.

The main drug classes used in the treatment of STEMI were registered in 1310 (98.1%) of the batch of patients included in the study. Overall, the rate of effective usage

was the following: 61.5% (statins) and 94.16% (anticoagulants) [Table 4]. Even more interesting seems to be the dynamics of the usage rate over the 10 years of study. During the specific period anticoagulant and antiplatelet drugs usage was quite constant, around 90%. ACE inhibitors and beta-blockers usage showed a first increase from 35% to 65% in the 2000 - 2005, period, while starting with 2006 the usage of the two classes showed evidence of a new increase up to 80% in 2008.

The most spectacular increase was registered for the usage of statins, from 31% in 2000, up to 94% in 2008. In the period of follow-up, the rate of usage suffered different shifts, comparing anticoagulants and blood platelet anti-agreggants. Thus, after 2002 enoxaparin gradually replaced unfractionated heparin.

TABLE 3

Analysis of major complications

Patients	dm	non-dm	„p"
No patients N=1335 (%)	278 (20.8%)	1057 (79.2%)	-
Killip class at admission N=1292 (96.7%)	269 (20.9%)	1023 (79.1%)	-
Killip 1 N=788 (60.9%)	80/269 (29.7%)	708/1023 (69.2%)	0.001
Killip2 N=208 (16.09%)	81/269 (30.1%)	127/1023 (12.4 %)	0.01
Killip 3 N=131 (10.1%)	60/269 (22.3 %)	101/1023 (9.8%)	0.001
Killip 4 N= 165 (12.7%)	48/269 (17.8%)	87/1023 (8.5%)	0.01
Cardiogenic shock N=24/1280 (1.9%)	16/259 (6.2%)	8/1021 (0.8%)	0.01
Killip III-IV + cardiogenic shock N=320/1335 (23.4%)	124/278 (44.6 %)	196 /1057 (18.5 %)	0.001
Failed fibrinolysis N=38/1335 (2.9%)	16/278 (5.8%)	22/1057 (2.1%)	0.05
AP-post AMI N=102/1280 (7.9%)	38/274 (13.8 %)	64/954 (6.7 %)	0.01
AP- fibrinolysis AMI N=70/1280 (5.4%)	26/274 (9.3%)	44/954 (4.6%)	0.01
AP-non fibrinolysis AMI N=32/1280 (2.5%)	12/274 (4.3%)	20/954 (2.1%)	0.05
Reinfarction N=15/1280 (1.1%)	5/274 (1.8 %)	10/954 (1.04 %)	NS
Major hemorrhage N=16/1280 (1.2 %)	5/274 (1.8 %)	11/954 (1.1 %)	NS
Total strokes N=15/1280 (1.1%)	4/274 (1.4 %)	11 /954 (1.1 %)	NS
Hemorrhage stroke N=7/1280 (0.5%)	2/274 (0.7 %)	5 /954 (0.5 %)	NS
Ischemic stroke N=8/1280 (0.6%)	2/274 (0.7 %)	6 /954 (0.6 %)	NS

Legend: DM-diabetes mellitus, No – number, SD-standard deviation, AMI-acute myocardial infarction, AP-angina pectoris

Beginning with 2006 a new tendency could be noticed, the usage of a combination of unfractionated heparin (applied during hospitalization in the Coronary Intensive Care Unit) and enoxaparin (prescribed as a follow up treatment after transfer outside the Coronary Intensive Care Unit).

Aspirin was practically the exclusive platelet antiaggregant drug used with patients enrolled until 2002. There was a rapid increase in the number of patients with whom dual antiaggregant drugs (Aspirin + Clopidogrel) were used. Thus, in 2008, 74% of these patients were receiving this specific combination.

Invasive therapy in patients formerly treated using conventional methods or thrombolytic occurred in very few cases as the hospital was lacking the necessary equipment. As the patients required transfer into other healthcare units, (closest, within a 150 km range distance), until 2005 coronarography was performed during the first 48 hours in merely 6% of them, increasing to 12% starting with 2008. There were no significant differences between therapeutic methods (conventional versus fibrinolytic), or between the main therapeutic classes applied in DM patients compared to non-DM ones, but with DM patients physicians encountered a much higher rate of unsuccessful fibrinolyses, 5.8% compared to 2.1% of fibrinolysis failures in patients without DM (p=0.05) (Table 3).

Major complications. The analysis of STEMI complications was limited to the following variables: cardiogenic shock, heart failure, early post-infarction angina, major hemorrhage, stroke, early reinfarction. The incidence of major complications was correctly reported in a number of 1280 patients (95.8%). Of these 24 (1.9%) were reported having developed cardiogenic shock after hospitalization: 15 (2.3%) belonged to the group that underwent conventional therapy, presenting 96.5 % (637 pts) correct entries and 9 (1.4%) to the group that received fibirinolysis, presenting 95.2% (643 pts) correct entries. In 296 patients (23.1%) symptoms of heart failure (Killip class III-IV) could be identified: 181 (28.4%) patients who underwent conventional therapy and 115 (17.8%) who received fibrinolysis (p<0.01). Early post infarction angina was present in 102 pts (7.9 %): 32 (5.02%) belonged to the group, which underwent conventional therapy and 70 (10.08%), to the batch that received fibrinolysis (p=0.01).

Reinfarction was reported in 15 patients (1. 1%); 8 (1.2%) belonged to the batch that received conventional therapy and 7 (1.08%) to the group which underwent fibrinolysis (p=NS). A group of 16 patients (1.2%) was reported to have suffered from major hemorrhage after hospitalization: 5 (0.8%) were patients who had conventional therapy and 11 (1.7%) those who had fibrinolysis (p=0.001).

A number of 15 patients developed stroke on admission (1.1%). In 7 of these patients (0.5%) the stroke was hemorrhagic: 1 patient (0.1%) underwent conventional therapy and 6 (0.9%) had fibrinolysis (p=0.001). A number of 8 patients (0.6%) had suffered an ischemic vascular event: 4 (0.6%) of the batch that had conventional therapy and 4 (0.6%) of the batch that had fibrinolysis (p=NS).

The analysis of the major complications was performed separately for DM and non-DM patients. Significant differences were recorded for all forms of heart failure (Killip class III-IV and cardiogenic shock): DM patients had a markedly higher incidence of heart failure episodes (44,6% vs. 18,5%, p=0.01).The number of recurrent angina episodes were higher in number in DM patients who received fibrinolysis, 9.3%, compared to 4.6% recorded in non DM patients (p=0.01). These differences were also maintained in DM and non-DM patients who not underwent fibrinolysis with a higher rate of recurrent angina in DM patients, 4.3% compared to 2.1% (p=0.05). On the other hand, no differences were recorded regarding the onset or evolution of ischemic or hemorrhagic vascular event complications (Table 3).

Mortality rate. Overall mortality rate in patients included in the study was of 15.3%: 19.4% in DM patients and 14.3% in non-DM patients (p=0.05). Mortality rate was significantly lower, 11.3% in those 539 non-DM patients who underwent fibrinolysis, compared to 16.5% in those 136 DM patients who received the same therapy (p=0.02) and to the 21.4% in those 142 DM patients who did not receive fibrinolysis (p<0.01; Table 5).

Analysis of the data included in the paper, required comparison with data reported by other registries. We referred to two well-known international registries, the Euro Heart Survey - EHS with its components I and II (Mandelzweig et al., 2006) and the Global Registry of Acute Coronary Events - GRACE, its European multinational counterpart (Kristen et al., 2004). We referred as well as the Romanian Registry Report for ST segment elevation Acute Myocardial Infarction RO – STEMI 1997-2008 (Tatu-Chitoiu et al., 2009). Between September 2000 and May 2001 EHS enrolled a number of 4431 STEMI patients from 103 centers distributed throughout 25 countries and in 2004 EH II enrolled 3004 patients from 190 centers and 32 countries. In the period between March – October, on its turn, GRACE included a number of 6425 STEMI patients coming from 94 centers in 14 countries.

TABLE 4

Characteristic and distribution of main therapeutic drugs classes

Patients	dm	NON-DM	„p"
No Patients N=1335 (%)	278 (20.8%)	1057 (79.2%)	-
Fibrinolytic N=675 (50.5%)	136 (48.9%)	439 (41.5%)	0.08
Anticoagulants N=1234/1310 (94.1 %)	251/270 (92.9 %)	983/1040 (94.5%)	NS
Antiaggregants N=1213/1310 (92.5%)	244/270 (90.7 %)	969/1040 (93.1%)	NS
IECA N=985/1310 (75.2 %)	215/270 (79.6 %)	770/1040 (74.1 %)	0.10
Beta-blockers N=890/1310 (68 %)	185/270 (68.5%)	705/1040 (67.7%)	NS
Statins N= 805/1310 (61.5%)	172/270 (63.7%)	633/1040 (60.8 %)	NS

Legend: DM-diabetes mellitus, No – number, IECA- inhibitors of angiotensin converting enzyme

Consequently, the data included in our study can be considered "contemporary" to those included in EHS I –II, GRACE and RO –STEMI. The mean age of our patients (64 years of age) was 1-2 years higher than in RO-STEMI and similar to the reported values in the other registries. The percentage of female patients included in our study, 33.1%, was similar to the RO-STEMI but higher, compared to 26-29% reported in the other registries. The 45.6% prevalence of arterial hypertension and 20.8% DM in our patients were similar to those registered by RO-STEMI and to those recorded in the Euro Heart Survey I and II for arterial hypertension. Regarding DM, its prevalence of was lower, compared to that of 24% reported in GRACE. The 48.7% prevalence of cigarette smoking was similar to that reported in RO-STEMI, but considerably higher than reported in the other registries, especially compared to the 34% reported by GRACE. On the other hand, the 43.5% prevalence of dyslipidemia was higher than in the RO-STEMI and GRACE studies, but lower than the values registered by EHS I and II. The 245 minute mean time that passed between the revealing symptoms of myocardial infarction and the moment of arrival to a emergency unit exceeded by 10 minutes the

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time reported by RO-STEMI, and by 25 minutes more than the time given in EHS I and 65 minutes more than that in EHS II.

This major difference can be explained partially by the well-known fact that Romanian patients show a tendency to seek medical help in a healthcare unit with a certain delay. It may also be attributed to the lack of interventional reperfusion techniques in our hospital, which cause paramedics not to realize how important it is to initiate fibrinolysis as soon as possible. Despite of that, the initiation of thrombolytic therapy registered a considerable increase from 41.6% in the period 2003 – 2008 (as recorded in RO-STEMI registry) to 50.6% and evidently double, compared to the values included in international registries, which record data collected for patients from countries predominantly applying interventional reperfusion strategies. This might be the explanation for the major differences in mortality rate, an overall value of 15.3%, higher than the 13.16% recorded by RO-STEMI, which, on the other hand included patients from medical centers possessing interventional techniques or better medical equipment, but with distressingly higher mortality rates than those communicated by international registries, which were of 5 – 8 %. We recorded a higher risk factor in patients included in our study: mean age 1-2 years higher, more frequent presence of dyslipidemia, an almost double number of, (10,4 % compared to 5,1%) prior history of myocardial infarction (possibly due to the fact that the hospital covers a number of approximately 500,000 inhabitants concentrated on a rather small area. We noted also more frequent cases of Killip class III and IV (22,3 % and 17,8%, compared to 9,8% and 8,5%) as well as more episodes of cardiogenic shock (6,2% vs. 0,8%; Table 3). The high mortality rate, compared to that recorded by international registries can also be explained by the lower percentage in administration of some medication : regarding the main therapeutic classes, (antiaggregants, anticoagulants, ACE inhibitors and beta-blockers) the percentage is very similar to that found in the RO-STEMI registry, but 10-20% lower than the percentage recorded in the international registries. Despite the fact that in the last 4 years drugs of the afore mentioned class have been prescribed in a markedly higher degree, according to the instructions given by the new guides for STEMI, it is only with statins that similar percentages were recorded right from the start.

The influence of DM in patients included in our study is primarily highlighted by the marked difference between the mortality and complications early post infarction. Mortality rate was different, depending on the presence or absence of DM. Overall mortality rate was reported as being 15.3% but it showed some difference between the subgroups, from 19.4% in DM patients to merely 14.3% in patients without DM ($p=0.05$). Mortality rate was markedly lower, of only 11.3% in those 593 non-DM patients who underwent fibrinolysis, compared to 16.5% recorded in 136 DM patients who underwent the same therapy, ($p=0.02$) and to 21.4% recorded in DM mellitus patients who did not undergo fibrinolysis ($p<0.01$) [Table 5]. In this respect the rate of major complications as well as that of high mortality rate values are similar to those reported in other studies, 21% versus 11% (Moreno et al., 2001) and 18 % versus 12 % (Koek et al., 2007). In addition, in our study, the aggravated prognosis for STEMI and DM patients finds an explanation in their worse clinical profile and the alteration of myocardial reperfusion, which is worse, reflected by a lower success rate of fibrinolysis and a higher recurrence rate of ischemia. The DM patients encountered a much higher rate of unsuccessful fibrinolyses, 5.8%, compared to 2.1% of fibrinolysis failures in patients without DM ($p=0.05$), as well a higher number of recurrent angina episodes after fibrinolysis, 9.3%, compared to 4.6 % recorded in non DM patients ($p=0.01$; Table 3).

It is also interesting to note that, although the results of the different studies are very similar, a number of authors attribute DM

patients' excessive mortality rate to underused pharmacological reperfusion (Gustafsson et al., 2000; Wong et al., 2000). Other authors think that the combination of their worse clinical profile and a more extended coronary affectation confirmed by angiography are responsible for the higher mortality rate (Zuanetti et al, 1993; Moreno et al, 1999; Kristen F., 2004). Our study, which does not include an angiographic comparison, but has used pharmacological reperfusion on a large scale, brings clinical evidence for a less documented hypothesis (Van't Hof et al., 2001), i.e. the worst influence of DM upon myocardial reperfusion manifested by an increased number of failures in thrombolysis, and more recurrent ischemia. An underdeveloped collateral circulation in DM patients, a well-documented hypothesis in some angiographic studies (Abaci et al., 1999) could also explain the higher rate of post-infarction ischemia and recurrent angina.

On the other hand, our study reconfirms that DM-STEMI patients had a worse clinical profile because, as demonstrated by other studies as well, they were of advanced age, preponderantly female, presented increased co morbidity and cardiovascular risk factors.

Afore mentioned clinical risk factors could explain the different mortality rates registered for DM patients without thrombolysis, 21.4%, compared to those DM patients who had fibrinolysis, whose mortality rate risk was markedly reduced, down to 16.5 %, compared to the merely 14.3 % of non-DM patients without fibrinolysis and the 11.3% non-DM patients who received fibrinolysis. The DM patients showed a marked tendency to have delayed presentations, of 12 – 24 hours, while those without DM sought medical help in the first 3 hours after the onset of symptoms and this fact could contribute to the over excessive mortality rate recorded in these patients (Table 2). Recent studies confirm the fact that DM remains an independent risk factor for short-term mortality subsequent to a first acute myocardial infarction, despite the ever-increasing preference for invasive reperfusion therapy as a treatment of AMI (Maier et al, 2006; Koek et al, 2007; Hansen H.H. et al, 2007).

Regarding other complications for all the clinical forms of heart failure (Killip class III – IV and cardiogenic shock) the DM patients significantly outnumbered the non-DM ones in episodes registered, 44.6% vs. 18.5% (p=0.001; Table 3). The respective risk had already been reported in other similar studies and it did not seem to have been attributed to differences regarding ejection fraction, hypertension, obesity, and a prior history of myocardial infarction, advanced age, techniques in testing hyperglycemia or other conditions responsible for triggering heart failure phenomena (SOLVD Trial., 1991).

TABLE 5

Mortality rate

Patients	dm	non-dm	„p"
No patients N=1335 (%)	278 (20.8%)	1057 (79.2%)	-
Overall mortality rate N=205/1335 (15.3%)	54 (19.4%)	151 (14.3%)	0.05
Mortality rate in patients who underwent fibrinolysis N= 83/675 (12.3%)	22/136 (16.5%)	61/539 (11.3%)	0.02
Mortality rate in patients with no fibrinolysis N= 108/660 (16.3%)	30/142 (21.4%)	78/518 (15.4 %)	0.01

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One of the mechanisms invoked by several investigators seems to be diabetic cardiomyopathy, apparently present and under diagnosed in the majority of patients (Lomuscio el al., 1991; Herlitz et al., 1998).

There is no major difference between therapies with anticoagulants, antiaggregants, beta-blockers or statins applied for DM patients whose treatment only show a favorable trend with which ACE inhibitors are administered, compared to non-DM patients (Table 4).

This is quite encouraging for the medical practice in our country and complies with the general global tendency. Unlike for other registries and especially the GRACE, thrombolysis was applied equally to DM and non-DM patients. Regarding the invasive treatment of DM patients, there is no significant difference between the two groups, opposed to the current tendency to perform early revascularization procedures in DM patients with a very high cardiovascular risk. (Van Belle et al., 2002). The explanation for all that derives from the lack of possibilities for invasive exploration in our hospital.

CONCLUSIONS

Methodological limitations regarding the influence of DM in patients included in our study are very important. The study has a retrospective character and the data included in it could not be validated for all the patients included. However, the presence of them in more than 85% of the patients excludes the risk of obtaining significantly altered results. On the other hand, the study has not had in view the analysis of some important data regarding glycemic control and the evolution of in-hospital glycemic index or the identification of all possible complications in the respective patients. We could not produce any data regarding the mortality rate depending on the therapy applied for DM or the evolution of the glycemic index. Despite all these drawbacks, the data obtained for DM patients who developed STEMI over the period of ten-year follow-up for the study are in perfect harmony with the results obtained by earlier or more recent studies and confirm the hypothesis that the presence of DM in patients with STEMI is an important risk factor for short-term mortality and morbidity.

The results obtained through the study highlight a markedly higher short-term mortality rate in patients with STEMI and DM, explainable, in the first place by a worse clinical profile and the alteration of myocardial reperfusion resulting in a lower success rate of fibrinolysis. This requires a more aggressive and comprehensive therapeutic management for the respective patients in order to substantially reduce cardiovascular morbidity and mortality

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