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Risk factors for post-acute myocardial infarction depression in elderly

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Abstract. Objective: To determine risk factors for development of post-acute ST elevation myocardial infarction (STEMI) depression in elderly. Material and Methods: We included 104 elderly patients diagnosed with STEMI. Clinical, lab and imagistic data was recorded in the first week after STEMI. Six months after STEMI patients were evaluated for the presence of depression. Results: Bivariate analysis showed statistically significant association between post-STEMI depression and sex, arterial hypertension, type 2 diabetes, socio-economic status, presence of family, left ventricular ejection fraction, Lown classification and HDL-cholesterol values. Multivariate analysis determined that following parameters increased the probability of onset of depression six months post-STEMI in elderly: sex (OR – 3.2), type 2 diabetes (OR – 2.6), poor socio-economic status (OR – 3.5) and absence of family (OR – 4.2). Conclusion: diabetes, precarious socio-economic status, absence of family and female sex were risk factors for post-STEMI depression.
Key Words: elderly, depression, acute myocardial infarction, risk factors.

Introduction. In last decades numerous studies had as objective the associative relation between cardiovascular diseases and depressive disorder (DD). The risk of DD occurrence after an acute coronary event was evaluated. The impact of post ST-elevation myocardial infarction (PSTEMI) DD determines the formation of a vicious circle with nefarious consequences upon patient's clinical evolution or short and medium prognostic. Trials that studied prevalence of PSTEMI DD had included mainly adults, so, few people over 65 years were present in them. As clinical depression in the elderly is a common finding and an increasing prevalence of STEMI is recorded, we decided to study the implication of some risk factors for onset of DD PSTEMI in the elderly.

To that purpose we tried to establish an independent association of some parameters with the occurrence of PSTEMI DD: sex, history of heart disease, arterial hypertension, diabetes mellitus, obesity, lipidic profile, smoking, patient's socio-economic status and presence of family. Also we studied the correlation of physiopathologic changes, induced by acute myocardial infarction, and DD: ejection fraction of left ventricle (LVEF), Killip classification and heart rhythm disturbances.

Material and method. The study took place between November 2005 and May 2009. The setting was Clinical Municipal Hospital of Cluj-Napoca. Patients were selected from those admitted in Cardiology or Geriatrics Department, following the signature of an informed consent form, in accordance with the protocol of "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca.

We included 104 patients aged over 65 years that were diagnosed with STEMI. Sex ratio was 1:1.4 (43 (41.3%) women and 61 (58.7%) men). Mean age was 76±6.1 years, and most frequently met age was 77 years. STEMI was diagnosed according to the

following criteria: history of chest pain/discomfort lasting for 10–20 min or more; persistent ST-segment elevation or (presumed) greater than 0.1 MV in at least 2 contiguous precordial leads (V1-V6) or at least 2 adjacent limb leads, new left bundle-branch block; elevated markers of myocardial necrosis (CK-MB, troponins); 2-D echocardiography to rule out major acute myocardial ischaemia or other causes of chest pain/discomfort (Van de Werf et al 2008). For echocardiography we used an Aloka SSD 4000 unit equipped with a microconvex transducer.

For every patient we recorded general data (age, sex, socio-economic status, family's presence, history of cardiovascular or psychiatric diseases, smoking status), clinical parameters and lab results. Socio-economic status was defined as "precarious" when patient's pension was less than 700 RON (about 160 euro) per month. Body mass index (BMI) was calculated and patients were classified accordingly (WHO 2000).

After we established the diagnosis of STEMI we evaluated the presence of arrhythmias with a 24 hours Holter ECG monitor (Schiller MT-101). We noted the presence of ventricular extrasystoles according to Lown classification (Lown et al 1975).

We used Killip classification in order to estimate severity of myocardial necrosis in regard to clinical signs of left ventricular failure (Killip & Kimball 1967). Using echocardiography we recorded LVEF and location of STEMI.

We determined blood values of total cholesterol (NV 140-200 mg dl^{-1}), HDL-cholesterol (NV > 40 mg dl^{-1} for men; > 50 mg dl^{-1} for women), LDL-cholesterol (NV <160 mg dl^{-1}) and triglycerides (NV 50-150 mg dl^{-1}) (Birtcher & Ballantyne 2004; Toth 2005).

In order to define and evidentiate DD diagnostic elements we used two scales: Beck Depression Inventory (BDI) and short version of Geriatric Depression Scale (GDS). However, in final analysis we only used the results produced by BDI, because GDS is not validated on a Romanian population (Yessavage et al 1987; Beck & Clark 1991). Also we applied the minimal state examination (MMSE) in order to evaluate patient's cognitive function. The tests were applied in the seventh day PSTEMI and at six month PSTEMI.

We included in study only patients that did not present depressive elements at first examination. Also we excluded patients with history of psychiatric diseases, stroke, Parkinson's disease, brain injury, alcoholism, neoplasm, end-stage renal disease and endocrine diseases. We did not included patients that had a score less than 21 at MMSE (medium and severe cognitive deficit).

Statistical analysis was performed using SPSS version 17 software. When appropriate we used t-test for independent variables, Mann-Whitney test, Spearman correlation and chi-square test. Multivariate analysis was performed using binary logistic regression. A P value, lower than 0.05, was considered significant.

Results. About 50 (48.1%) patients came from a rural setting and 54 (51.9%) lived in cities. Although the study included more men than women, there was no difference regarding sex in demographic, clinical or lab data (chi-square tests).

History of ischemic heart disease was present in 72 (69.2%) patients. We determined a positive small correlation between patients' age and history of heart ischemia (Spearman correlation; $r=0.348$; $p<0.001$). Arterial hypertension was found in 41 (39.4%) subjects. Type 2 diabetes was found in 24 (23.1%) patients. Class I obesity was recorded in 16 (15.4%) patients and class II in 12 (11.5%) subjects.

About 33 (31.7%) patients had an adequate socio-economic status, but 71 (68.3%) patients had a precarious one. We determined the fact that patients with advanced age were living in poor conditions (Spearman correlation; $r=-0.382$; $p<0.001$). Urban or rural life setting were not associated with socio-economic status (chi-square test; $p<0.001$). Family was present in patient's life in 72 (69.2%) cases. Mean age of patients with family was less than that of lonely subjects (68.2±11.1 vs. 76±11.6) (t-test; $p=0.002$). There was no link between life setting and presence/absence of family (chi-square test; $p=0.42$). Approximately 30 (28.2%) patients were smokers previous to the occurrence of STEMI.

After six month from STEMI we diagnosed DD in 38 (36.5%) patients. Relationship between DD and several clinical, imagistic and lab parameters can be seen in table 1.

Table 1

Bivariate analysis for DD and several parameters

	Patients with DD (38)	*Patients without DD (71)*	*P*
Age (mean ± standard deviation)	77.7±6.23	75.62±6.63	0,1*
Women	22	21	0.01**
Men	16	45	
Urban home	19	19	0.92**
Rural home	35	31	
History of ischemic heart disease	30	42	0.15**
Arterial hypertension	21	20	0.02**
Systolic arterial pressure (median)	145 mm Hg	130 mm Hg	0.002***
Diastolic arterial pressure (median)	95 mm Hg	80 mm Hg	<0.001***
Diabetes	15	9	0.006**
Obesity (classification)			
I	7	9	
II	3	9	0.59**
Current smoker	12	18	0.8**
Adequate socio-economic status	14	57	<0.001**
Presence of family	19	59	<0.001**
Killip classification			
I	2	19	
II	18	27	<0.001**
III	18	20	
LVEF (median)%	35%	38%	0.003***
Lown classification			
I	9	7	
II	14	3	<0.001***
III	2	4	
Total cholesterol(mean ± standard deviation)	195.1±31.5 mg dl^{-1}	204±37.8 mg dl-1	0.22*
HDL-cholesterol (mean ± standard deviation)	46,16±10,7 mg dl-1	52±11,3 mg dl-1	0.01*
LDL-cholesterol (mean ± standard deviation)	145,1±30,5 mg dl-1	145,7±36.7 mg dl-1	0.93*
Triglycerides (median)	135 mg dl-1	144 mg dl-1	0.08

* T-test
** Chi-square test
*** Mann-Whitney test

Twenty one (20.2%) patients were included in Killip class I, 45 (43.4%) in class II and 38 (36.5%) in class III. We determined a small negative correlation between age and LVEF (Spearman correlation; r=-0.230; p=0.01). In the first week after STEMI we

recorded the presence of ventricular extrasystoles in 39 (37.5%) patients and supraventricular extrasystoles in 7 (6.7%) patients. Ventricular extrasystoles from Lown class I were detected in 16 (15.4%) patients, from class II in 17 (16.3%) patients and from class II in 6 (5.8%) patients.

Mean value of total cholesterol was 200.7±35.7 mg dl-1, of HDL-cholesterol was 49.9±11.4 mg dl-1, of LDL-cholesterol was 145.5±34.4 mg dl-1 and median of triglycerides was 141 mg dl-1.

We obtained a small positive correlation between Killip classes and PSTEMI DD, which means that patients that are included in a higher Killip class had a greater probability to develop DD (Spearman correlation; r=0.256; p=0.009). Values of LVEF were negatively correlated with presence of DD six months PSTEMI (Spearman correlation; r=-0.305; p=0.002).

We did not found a correlation between DD and total cholesterol or LDL-cholesterol, but we determined a small negative correlation between HDL-cholesterol and DD (Spearman correlation; r=-0.247; p=0.01).

In order to examine the independent implication of every parameter on the presence of DD six months PSTEMI, we used a binary logistic regression. We build several models, including variables previously studied, and in the end we included those parameters which produced the most stable model (table 2).

Table 2

Logistic regression for independent predictors of PSTEMI DD in elderly

Variables	*B*	*S.E.*	*Wald*	*df*	*P*	*OR*	*95% C.I.*	
							Min	*Max*
Age	-.184	.412	.199	1	.656	.832	.371	1.866
Women	1.163	.408	8.151	1	.004	3.201	1.440	7.114
Ventricular extrasystoles	1.136	.419	7.351	1	.007	3.114	1.370	7.079
Type 2 diabetes	.966	.438	4.870	1	.027	2.627	1.114	6.196
HDL-cholesterol	-.020	.033	.352	1	.553	.981	.919	1.046
LDL-cholesterol	.014	.012	1.227	1	.268	1.014	.990	1.038
Precarious socio-economic status	1.268	.507	6.260	1	.012	3.554	1.316	9.597
Absence of family	1.452	.490	8.763	1	.003	4.270	1.633	11.164

Value of Nagelkerke R2 was 0.692 and Cox & Snell was 0.506. Risk of PSTEMI DD was elevated for women (OR - 3.2). Ventricular extrasystoles raised the risk for DD by 3.1 times. Poor socio-economic status was associated with increased risk of DD (OR – 3.5). Absence of family raised risk of DD by 4.2 times.

Discussions. The fact that the link between DD and heart disease is often considered a predictable manner of interrelation, which leads frequently to neglecting of the first one, requires a well-defined hierarchy. As result, neglecting of implication and consequences generated by DD upon heart disease, may determine aggravation and self-maintaining of this vicious circle.

Our study showed that about one third (36.5%) of the patients that suffered STEMI developed DD six months after the cardiac event. This data is in accordance with medical literature (Naqvi et al 2007). On the other hand data analysis demonstrated that a series of clinical, lab and social parameters can be predictors for the onset of DD.

Implication of stress in DD pathogenesis can be analyzed from several perspectives. Therefore, stress can create a high susceptibility for pathologic modification that may initiate the circle of physiopathologic events or may exacerbate initial psychopathology. The role of psychological trauma was mentions by many authors which studied the impact of these events upon human psyche (Cohen & Wills 1985; Brown

1989). These researchers showed a significant increase of morbidity risk in case of exposure to different stressors of fluctuating intensity. Majority of studies seem to indicate the fact that onset of psychiatric diseases follow one of two models: the disease appears after one singular sudden traumatic event (macrotrauma theory), or it emerges after a long string of unpleasant, repetitive, low intensity experiences (microtrauma theory) (Chrousos & Gold 1992). Presently it is considered that in disease's pathogenesis the important factors are not just the number or intensity of life events, but individual significance that is attributed to them and psychological status of the person (Belar et al 1997). Age, through psychological, immunological, metabolic, circulatory frailty, constitutes an important predictor for DD. Impairment of cognitive functions and affectivity disorders are the most frequent changes that characterize advanced age (Ghidrai 2002).

In our study women were at a greater risk for develop DD six months PSTEMI than men (OR – 3.2). Previous trials, which included younger adults, found that women had elevated risk for PSTEMI DD, compared to men, although intrinsic mechanisms are not clearly defined (Frasure-Smith et al 1999; Malliket al 2006; Naqvi et al 2007; Parashar et al 2009). Although other studies on PSTEMI showed that socio-economic status was somewhat lower in women than in men, our data din not revealed such a correlation (Mendes de Leon et al 2001; Sapolsky 2002). A major cardiovascular trauma such as STEMI can trigger easily DD in women, rather than men (Brown 1993). Also women show a tendency to minimize emotional outbursts, therefore medical addressability is lower (Fielding 1991).

Type 2 diabetes is another factor that seems to be implicated in onset of PSTEMI DD (OR - 2.6). In previous decades studies have shown that adult with type 2 diabetes develop DD during the course of disease (Gavard et al 1993; Lustman et al 1997; Talbot & Nouwen 2000). Two hypotheses try to explain this correlation: first one state that biochemical changes that appear during natural course of diabetes or that are determined by medication may predispose to depressive symptoms; second one indicates that psychological and psychosocial factors that interfere with diabetes can favor onset of DD (Lustman et al 1997; Talbot & Nouwen 2000). According to first hypothesis, mechanisms by which diabetes may determine DD are related to changes in serotonin and cerebral catecholamine's levels, but also to glycemic control impairment (Goodnick et al 1995). Lustman et al (1997) proved that nortriptyline influences glycemic equilibrium as well as favorable effects upon psyche. Good psyche leads to a better compliance to treatment and an improved physical activity which explains a better glycemic control in diabetic patients with DD. Power & Snoek (2001) showed a correlation between depression and levels of glycated hemoglobin in women. Other studies demonstrated, by means of MRIs, that cerebral microvascular ischemia is common in patients with diabetes and DD (Raj 2004). These lesions determine cerebral degeneration with full spectrum of signs and symptoms specific for depression (Miller et al 2002). In a study of correlation between acute coronary syndrome and PSTEMI DD, Naqvi et al (2007) revealed diabetes as risk factor for depression.

Variations of heart rate are an important parameter for STEMI patients. Variations of heart rate are clinically represented by arrhythmias and changes in LVEF. In our study, presence of ventricular extrasystoles in the first week PSTEMI, as well as low LVEF, was correlated with DD. There are studies that prove the link between changes in heart rate and symptoms of depression (Carney et al 2005). Neuropeptide Y is the underline explanation of this association. It is responsible for sympathetic nervous system activity and it is implicated in onset of some psychiatric disorders (Podrid et al 1990).

Elders that had at least one family member in their lives were rarely diagnosed with PSTEMI DD in our study. The absence of family was the most powerful predictor for onset of post-infarction depression (OR – 4.2). Also we observed that people with advanced age were more likely to be lonely.

Socio-economic status was also an important risk factor for depression. Precarious material status was link to predisposition toward DD (OR - 3.5). This factor influences

greatly a person's life quality. In case of a sick lonely elder lack of money and social isolation can be responsible for psycho-affective degradation with a marked tendency for increased depressive symptomatology. This aspect favors the entrance into a vicious circle of lack of interest towards his person and disease, poor treatment compliance and finally death wish.

Conclusions. PSTEMI DD was a frequent finding in elderly. Women and patients with diabetes were more prone to develop this depression. Socio-economic status and presence of family were important predictors for onset of DD. These facts show that we must pay close attention to elderly that have suffered a major cardiac event in order to prevent and treat in time any symptoms or signs related to depression.

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