Predictor value of some clinical-biological parameters for the onset of depressive disorder in elderly patients with unstable angina

[1]Cristina Moşuţan, [2]George Săraci, and [3]Caius R. Duncea

[1] University Hospital C.F. of Cluj-Napoca, Cluj, România; [2] Third Medical Clinic (Regional Institute of Gastroenterology and Hepatology),"Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Cluj, Romania; [3] Fifth Medical Clinic, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Cluj, România

Abstract. Abstract. Objective: To evaluate the potential predictor value of some parameters for the onset of depression after an episode of unstable angina in elderly. Material and Methods: We included 103 elderly patients who suffered an acute unstable angina episode. Clinical, lab and imagistic data was recorded in the first week after admittance. Six month after unstable angina episode, patients were evaluated for the presence of depression. Results: Univariate analysis showed statistically significant association between depression and age, personal history of myocardial infarction, arterial hypertension, type 2 diabetes, inadequate socio-economic status, absence of family, left ventricular ejection fraction, LDL- and HDL-cholesterol values. Multivariate analysis showed that following clinical-biological parameters increase the probability of onset of depression six months after an unstable angina episode: history of myocardial infarction (OR, 12.8) and arterial hypertension (OR, 5.9). Adequate socio-economic status (OR, 0.145) and high levels of HDL-cholesterol (OR, 0.101) were considered protectors for onset of depression. Conclusion: Several factors, like arterial hypertension or history of myocardial infarction, may increase the risk of depression in elderly. High levels of HDL-cholesterol and adequate socio-economic status can prevent the onset of depression in patients that suffered an unstable angina episode.

Key Words: elderly, depression, unstable angina, predictors.

Corresponding Author: C. Moşuţan, cristinamosutan@yahoo.com.

Introduction

The relation between acute coronary disease, myocardial infarction to be exact, and depressive disorder is well known and studied in trials with adults, but it is less studied in elderly. More so, unstable angina, which is present at 26% of elderly hospitalized for acute coronary syndrome, can be a trigger for onset of depressive disorder (Whang *et al* 2010).

The high frequency of acute coronary disease in elderly and their predisposition to develop depression are well-known facts. We tried to establish if there is an independent association between some clinical-biological parameters frequently met in people with unstable angina and the onset of depression: sex, history of myocardial infarction, arterial hypertension, diabetes mellitus, obesity, dyslipidemia, smoking, socio-economic status, presence of family. Also we study the correlation between ejection fraction of left ventricle (LVEF) and the presence of depressive disorder.

Material and Method

The study took place between November 2005 and May 2009. Patients were selected from those admitted in Cardiology or Geriatrics Department of Clinical Municipal Hospital of Cluj-Napoca, 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 103 patients aged over 65 years that were diagnosed with unstable angina. Sex ratio was 1:1.14 (48 (46.6%) men and 55 (53.4%) women). Mean age was 73.46±5.5 years, and most frequently met age was 68 years.

Unstable angina was diagnosed according to the following criteria (Braunwald *et al* 2011): 1) severe retrosternal chest pain characteristic to coronary disease which appears at rest or minimal effort, is 20 minutes long or presence of anginal equivalent (progressive dyspnea, epigastric or pleural pain); 2) specific changes of ST segment: depressed ST segment by minimum 0.05 mV or transitory elevation of ST segment by at least 0.1 mV in at least two adjacent derivations; 3) negative, symmetrical, sharp T waves >0.3 mV (>2 mm); 4) no increase in levels of T troponin or creatine kinase-MB; 5) transitory Q waves. For echocardiography we used an Aloka SSD 4000 unit equipped with a microconvex transducer.

Data recordings, diagnosis of depression and exclusion criteria were described in a previous paper (Moşuţan *et al* 2011). Tests used for diagnosis of depression were applied in the seventh day post admittance for an angina episode and at six months after discharge.

Table 1. Univariate analysis for depression and several parameters

Variables	Patients with depression (25)	Patients without depression (80)	P
Age (mean ± standard deviation)	75.9±5.4	72.6±5.3	0.01[*]
Women	17	38	0.14[**]
Men	8	40	
Urban home	10	38	0.44[**]
Rural home	15	40	
History of myocardial infarction	12	13	0.001[**]
Arterial hypertension	19	6	0.007[**]
Diabetes	12	13	0.004[**]
Obesity	6	19	0.3[**]
Current smoker	11	14	0.88[**]
Adequate socio-economic status	9	16	<0.001[**]
Presence of family	9	16	<0.001[**]
LVEF (median)%	35%	42%	<0.001[***]
Total cholesterol(mean ± standard deviation)	223±35.2 mg dL^{-1}	198.5±32.8 mg dL^{-1}	0.38[*]
HDL-cholesterol (mean ± standard deviation)	43.9±6.7 mg dL^{-1}	60.6±9.1 mg dL^{-1}	<0.001[*]
LDL-cholesterol (mean ± standard deviation)	160±36.2 mg dL^{-1}	142.5±30 mg dL^{-1}	0.04[*]
Triglycerides (median)	120 mg dL^{-1}	117 mg dL^{-1}	0.98[***]

[*] T-test

[**] Chi-square test

[***] Mann-Whitney test

Table 2. Logistic regression post unstable angina depression

Variables	B	S.E.	Wald	df	P	OR	95% C.I. Min	95% C.I. Max
Age	0.17	0.106	2.568	1	0.109	1.185	0.963	1.459
Sex	-1.678	1.55	1.172	1	0.279	0.187	0.009	3.897
History of myocardial infarction	2.551	1.632	2.442	1	0.05	12.815	0.523	314.072
Diabetes	0.738	0.52	2.009	1	0.156	2.091	0.754	5.799
Arterial hypertension	1.783	0.817	4.765	1	0.029	5.948	1.2	29.491
Adequate socio-economic status	-1.933	0.819	5.567	1	0.018	0.145	0.029	0.721
Presence of family	0.016	0.629	0.001	1	0.98	1.016	0.296	3.485
HDL-cholesterol	-2.293	0.767	8.923	1	0.003	0.101	0.022	0.455

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. The level of statistical significance was set at p<0.05.

Results

After six month from unstable angina episode we diagnosed depression in 25 (24.2%) patients. Relationship between depression and several clinical, imagistic and lab parameters can be seen in table 1.
We applied a Spearman correlation and we found a weak positive correlation between age and presence of depression six months after unstable angina episode (r=0.255; p=0.009). We did not found a correlation between depression and total cholesterol or triglycerides. We determined a strong negative correlation between HDL-cholesterol and depression (Spearman correlation; r=-0.623; p<0.001) and weak positive correlation between LDL-cholesterol and depression (Spearman correlation; r=0.199; p=0.04).

In order to examine the independent implication of several parameters on the presence of depression six months after an unstable angina crisis, 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). Value of Nagelkerke R2 was 0.834 and Cox & Snell was 0.559. Risk of post unstable angina depression was elevated in patients with history of myocardial infarction (OR - 12.8). Arterial hypertension increased the odds

for depression by 5.9 times. Adequate socio-economic status and high HDL-cholesterol levels decrease the odds for post unstable angina depression (OR – 0.145; respectively - 0.101).

Discussions

Our study demonstrates the existence of a link between some studied parameters and the onset of depression six months after an episode of unstable angina in elderly patients. In univariate analysis the following variables were associated with post angina depression: history of myocardial infarction, arterial hypertension, diabetes, precarious socio-economic status, absence of family, low LVEF, low HDL-cholesterol and high LDL-cholesterol. Multivariate analysis showed that only history of myocardial infarction, arterial hypertension, adequate socio-economic status and high levels of HDL-cholesterol had an independent contribution on the onset of depression post unstable angina episode.

We diagnosed depression six months after unstable angina diagnosis in 24.2% patients. Data from Nation Health Interview Survey, which enrolled over 30000 subjects, showed an annual prevalence of major depression of 9.3% in cardiovascular patients. In people without cardiovascular diseases the prevalence was 4.8% (Egede *et al* 2007). The prevalence rises in patients with severe cardiac pathologies (heart failure, myocardial infarction, unstable angina). Regarding elderly, Adamis et al determined the fact that depressive patients were more likely to have cardiovascular diseases, especially arterial hypertension and coronary disease (Adamis *et al* 2000).

In medical literature the incidence of post unstable angina depression is approximately equal with the one post-acute myocardial infarction: 20% (Lesperance *et al* 2000; Friedman & Griffin 2001). In a study that analyzed the onset of depression in adult that suffered an acute coronary event, Awaad et al determined that depression appeared in 40% of patients with unstable angina (Awaad *et al* 2010). Depression and coronary disease have in common several aspects. A theory, based on a vascular cause of depression, offers an explanation suited for elderly. Alexopoulos et al, Krishan and McDonald demonstrated that depression is accompanied in most of the cases by atherosclerosis of brain vessels and that this fact is most evident in patients with atherosclerotic coronary lesions. (Alexopoulos *et al* 1997; Krishan & McDonald 1997). Vascular changes which can lead to depression are endothelial dysfunction, reduced vasodilatation and low levels of nitric oxide metabolites (Parissis *et al* 2007). History of myocardial infarction was present in 22.3% patients in our study. This factor was the most powerful predictor of depression in our study (OR – 12.8). Studies showed that depression is three times more frequent in patients that suffered a myocardial infarction, as compared with general population. Schrader et al determined the fact that history of coronary disease rises the risk for moderate/severe depression (OR – 2) and for mild depression (OR – 2.3) at three months after a myocardial infarction, unstable angina, severe arrhythmias or heart failure (Schrader *et al* 2004). Approximately 65% of patients that suffers myocardial infarction present symptoms of depression, and major depression can appear in 22% of cases (Carney *et al* 1997). Kaptein et al demonstrated that the incidence of depression is relatively the same after myocardial infarction (23.8%) and unstable angina (24.8%) (Kaptein *et al* 2006). Biological

mechanisms and behavior models were proposed in order to explain the link between cardiac disease and depression. Cardiac patients which developed depression had high levels of markers of atherosclerosis, as compared with those that did not become depressed. Several studies showed a high sympathetic and reduced parasympathetic activity, dysfunctions of hypothalamic–pituitary–adrenal axis, early thrombocytes activation, endothelial dysfunction and high proinflammatory activity (CRP, Il-6, fibrinogen) (Pollock *et al* 2000; Carney *et al* 2001; Lespérance *et al* 2004; Empana *et al* 2005; Taylor *et al* 2006).

Arterial hypertension was another predictor for depression in elderly with unstable angina (OR – 5.9). Arterial hypertension is a major public problem. It is present in over 77% of depressive patients (Cankurtaran *et al* 2005). Some studies revealed the common element of hypertension and depression: cortisol hormone. Cortisol hypersecretion is responsible of vasoconstriction that predisposes people at risk to develop arterial hypertension. In depressive patients there is also a higher production of cortisol. Majority of studies proved hypertension role in the onset of depression in elderly (Argyriadou *et al* 2001; Cankurtaran *et al* 2005; Ried *et al* 2006). In contrast, HUNT study did not proved the fact that hypertension is linked with depression (Sung 2011).

High levels of HDL-cholesterol protected angina patients' form developing depression. Depression is associated with metabolic syndrome (Raikkonen *et al* 2007). Recent studies showed the other side of the coin: metabolic syndrome is a risk factor for depression (Almeida *et al* 2009). Three-City study reported a two time increase in risk of depression in elderly patients with metabolic syndrome. The only component that was independently linked with depression was the low value of HDL-cholesterol (Akbaraly *et al* 2011). ESPRIT study determined an association between depression and dyslipidemia (Ancelin *et al* 2010). The mechanism by which low HDL-cholesterol levels raise the risk for depression can be explained by the relation between polyunsaturated fatty acids and HDL-cholesterol. A diet lacking polyunsaturated fatty acids is associated with low levels of HDL-cholesterol. European Society of Cardiology guideline states that there are increases of HDL-cholesterol levels following a therapy with statins in combination with omega-3 fatty acids (Reiner *et al* 2011). Omega-3 fatty acids are major constituents of synaptic membrane and have an important role in central nervous system activity. Study that investigated the implication of omega-3 fatty acids in the onset of depression proved that major depressive disorder can be caused by an unbalanced diet. Serotonin released from thrombocytes is inhibited by polyunsaturated fatty acids. So a low level of fatty acids alters the homeostasis of this neurotransmitter which can trigger the depressive disorder (Mrowka *et al* 2000).

Conclusion

Depressive disorder following unstable angina is a common found in elderly. There are several factors, like arterial hypertension or history of myocardial infarction which can increase the risk of depression in elderly. High levels of HDL-cholesterol and adequate socio-economic status can prevent the onset of depression in patients that suffers from unstable angina.

References

Adamis, D., Ball, C., 2000. Physical morbidity in elderly psychiatric inpatients: Prevalence and possible relations between the major mental disorders and physical illness. Int J Geriatr Psychiatry 15(3):248-253.

Akbaraly, T. N., Ancelin, M. L., Jaussent, I., Ritchie, C., Barberger-Gateau, P., Dufouil, C., et al, 2010. Metabolic syndrome and onset of depressive symptoms in the elderly: findings from the three-city study. Diabetes Care 34(4):904-909.

Almeida, O. P., Calver, J., Jamrozik, K., Hankey, G. J., Flicker, L., 2009. Obesity and metabolic syndrome increase the risk of incident depression in older men: the health in men study. Am J Geriatr Psychiatry 17(10):889–898.

Alexopoulos, G. S., Meyers, B. S., Young, R. C., Campbell, S., Silbersweig, D., 1997. Vascular depression hypothesis. Arch Gen Psychiatry 54:915–922.

Ancelin, M. L., Carrière, I., Boulenger, J. P., Malafosse, A., Stewart, R., Cristol, J. P., 2010. Gender and genotype modulation of the association between lipid levels and depressive symptomatology in community-dwelling elderly (the ESPRIT study). Biol Psychiatry 68(2):125-132.

Argyriadou, S., Melissopoulou, H., Krania, E., Karagiannidou, A., Vlachonicolis, I., Lionis, C., 2001. Dementia and depression: two frequent disorders of the aged in primary health care in Greece. J Fam Pract 18:87–91.

Awaad, M., Darahim, K., 2010. Depression post-acute coronary syndromes: incidence and predictors. Egypt Heart J 62(1):173-179.

Braunwald, E., Cannon, C. P., 2012. CHAPTER 56 – Unstable Angina and Non–ST Elevation Myocardial Infarction, in Bonow, R. O., Mann, D. L., Zipes, D. P., Libby, P. (eds.), Braunwald's Heart Disease. A Textbook of Cardiovascular Medicine; 9th, Elsevier Saunders, Edition, Philadelphia, p. 1178.

Cankurtaran, M., Halil, M., Yavuz, B. B., Dagli, N., Cankurtaran, E. S., Ariogul, S., 2005. Depression and concomitant diseases in a Turkish geriatric outpatient seting. Arch Gerontol Geriatr 40:307-315.

Carney, R. M., Freedland, K. E., Sheline, Y. I., Weiss, E. S., 1997 Depression and coronary heart disease: a review for cardiologists. Clin Cardiol 20:196–200.

Egede, L. E., 2007 Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. Gen Hosp Psychiatry 29:409–416.

Empana, J. P., Sykes, D. H., Luc, G., Juhan-Vague, I., Arveiler, D., Ferrieres, J., et al, 2005 PRIME Study Group. Contributions of depressive mood and circulating inflammatory markers to coronary heart disease in healthy European men: the Prospective Epidemiological Study of Myocardial Infarction (PRIME). Circulation 111: 2299–2305.

Friedman, M. M., Griffin, J. A., 2001. Relationship of physical symptoms and physical functioning to depression in patients with heart failure. Heart Lung 30:98-104.

Kaptein, K. I., Jonge, P., Brink, R. H. S., Korf, J., 2006. Course ofDepressive Symptoms After Myocardial Infarction and Cardiac Prognosis: A Latent Class Analysis. Psychosomatic Medicine 68:662-668.

Krishnan, K. R. R., McDonald, W. M., 1995. Arteriosclerotic depression. Med Hypotheses 44:111–115.

Lesperance, F., Frasure-Smith, N., Juneau, M., Theroux, P., 2000. Depression and 1-year prognosis in unstable angina. Arch Intern Med 160:1354–1360.

Moşuţan, C., Diaconu, R. E., Rădulescu, M. L., Şerban, A. M., Duncea, C. R., 2011. Risk factors for post-acute myocardial infarction depression in elderly. HVM Bioflux 3(3):220-226.

Mrowka, R., Persson, P. B., Theres, H., Patzak, A., 2000. Blunted arterial baroreflex causes pathological heart rate turbulence. Am J Physiol Regulatory Integrative Comp Physiol 279:R1171–5.

Parissis, J. T., Fountoulaki, K., Filippatos, G., Adamopoulos, S., Paraskevaidis, I., Kremastinos, D., 2007. Depression in coronary artery disease: novel pathophysiologic mechanisms and therapeutic implications. Int J Cardiol 116(2):153-160.

Pollock, B. G., Laghrissi-Thode, F., Wagner, W. R., 2000. Evaluation of platelet activation in depressed patients with ischemic heart disease after paroxetine or nortriptyline treatment. J Clin Psychopharmacol 20:137–140.

Raikkonen, K., Matthews, K. A., Kuller, L. H., 2007. Depressive symptoms and stressful life events predict metabolic syndrome among middle-aged women: a comparison of World Health Organization, Adult Treatment Panel III, and International Diabetes Foundation definitions. Diabetes Care 30(4):872–877.

Reiner, Z., Catapano, A. L., De Backer, G., et al, 2011. ESC/EAS Guidelines for the management of dyslipidaemias: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Eur Heart J 32:1769–1818.

Ried, L. D., Tueth, M. J., Taylor, M. D., Sauer, B. C., Lopez, L. M., Pepine, C. J., 2006. Depressive symptoms in coronary artery disease patients after hypertension treatment. Ann Pharmacother 40:597–604.

Schrader, G., Cheok, F., Hordacre, A., Guiver, N., 2004. Predictors of Depression Three Months after Cardiac Hospitalization. Psychosomatic Medicine 66:514-520.

Sung K., 2010. Factors associated with depressive symptoms in low-income, older Korean women with hypertension. Nursing and Health Sciences 13:309-315.

Taylor C. B., Conrad, A., Wilhelm, F. H., Neri, E., DeLorenzo, A., Kramer, M. A., et al, 2006. Psychophysiological and cortisol responses to psychological stress in depressed and nondepressed older men and women with elevated cardiovascular disease risk. Psychosom Med 68:538–546.

Whang, W., Shimbo, D., Kronish, I. M., Duvall, L.W., Julien, H., Iyer, P., et al, 2010. Depressive Symptoms and All-Cause Mortality in Unstable Angina Pectoris (from the Coronary Psychosocial Evaluation Studies [COPES]. Am J Cardiol 106;1104-1107.

Authors

•Cristina Moşuţan, University Hospital C.F. of Cluj-Napoca, 16-20th Republicii Street, 400015, Cluj, Românía, EU, email: cristinamosutan@yahoo.com.

•George Săraci, Third Medical Clinic (Regional Institute of Gastroenterology and Hepatology),"Iuliu Haţieganu" University of Medicine and Pharmacy, 19-21st Croitorilor Street, 400162, Cluj-Napoca, Cluj, Romania, EU, gsaraci@yahoo.com

•Caius Romulus Duncea, Fifth Medical Clinic, "Iuliu Haţieganu" University of Medicine and Pharmacy 11th Tăbăcarilor Street, 400139, Cluj-Napoca, Românía, EU, email: crduncea@yahoo.com