Biopsychosocial implications of depression and cognitive deficit in elderly patient PhD Thesis Abstract

SCIENTIFIC COORDINATOR:

Prof. Univ.Dr. ŞTEFĂNESCU CRISTINEL

Prof. Univ.Dr. TURLIUC MARIA-NICOLETA- "Alexandru Ioan Cuza" University of Iași

Phd student

CIOBĂNEL (căs. BODESCU) MARIA-MĂDĂLINA

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ABBREVIATIONS LIST

ACTH-Adrenocorticotropic Hormone

CRP-C Reactive protein

CT-Computer Tomograph

DS - Standard deviation

DSM-Diagnostic and Statistical Manual of Mental Disorders

DST-dexamethasone suppression test

EKG-Electrocardiogram

GABA-gamma-aminobutyric acid

GDS-The scale of geriatric depression

GGT-Gamma-Glutamyltranspeptidaza

GIM-Average Intimate Thickness

GR-glutathione reductase

HDRS-HAMILTON Depression Assessment scale

HTA-High blood pressure

IGB-Arm Ankle Index

MMSE-Mini Mental State Examination

MPHG-3-methoxy-4 Hydroxyphenylglycol

RDAS-Revised dyadic adjustment scale

MRI-Magnetic nuclear resonance

ROS-Oxygen Reducer species

CNS-Central nervous system

SOD-superoxide dismutase

STH-Somatotropic Hormone

TA-blood pressure

TGO-transferase Glutamooxalacetics

TGP-transaminase Glutam Piruvic

The doctoral thesis has 221 pages and includes 77 figures,142 tables, and 414 references. The table of contents, list of abbreviations, and the numbers of selected tables and figures are similar to those in the thesis.

PERSONAL PART

CHAPTER VI

STUDY AND CLINICAL-BIOLOGICAL CORRELATIONS IN DEPRESSION-COGNITIVE STATUS AT ELDERLY PATIENTS

6.1 Study prestakes

Almost 25% of people over 65 years of age experience depressive and cognitive disorders (Kokmen et al., 1991, Koenig et al., 1992). Studies have shown in recent years possible correlations between the two pathologies, both with a high frequency among elderly patients. The combination of depression cognitive dysfunction is known in literature, the similarities existing at the level of the clinical and neurocognitive panel of depression and early dementia in the elderly raises problems of differential diagnosis (Popescu et al., 1994). The identification of some indices that can guide the early differential diagnosis is necessary for the shaping of the therapeutic plan and the formulation of the prognosis. Studies have shown the presence of deficits in executive functions since the early stages of Alzheimer's dementia (Perry et al., 1999, Hodges, Miller. 2001), the impairment of these functions was also reported to depression, in general, and in the elderly, in particular. Affections of visual or verbal functions in depression have also been demonstrated (Abas et al., 1990; Brown et al., 1968, Beats et al., 1996), deficits of these functions also occurring in dementia. With the older submission of information processing resources to reduce and this fact negatively influences the processes and intellectual activities, in normal elderly people to decrease the processing resources of Information largely explains the decline in cognitive evidence, from episodic memory to problem solving.

6.2 Purpose of the study

Research has proposed to identify the correlation between depression and cognitive dysfunction in third-age individuals, establishing the qualitative ratio of depression with decreased cognitive efficiency and their association with the presence of cardiovascular risk factors and the default cardiovascular disease.

The research was conducted in two stages.

The first stage (Study takes Clinico-biological correlates cardiovascular risk factors Depression-cognitive status in elderly patients):

- -Studying the relationship between some cardiovascular risk factors, biochemical, anthropometric, socio-demographics and normal cognitive ageing.
- -Studying the relationship between some cardiovascular risk factors, biochemical, anthropometric, socio-demographics and depression.
- -Study of the relationship between some cardiovascular risk factors, biochemical, anthropometric, socio-demographics and cognitive disturbances in 4 batches of patients diagnosed or not with various forms of cognitive disorder and cardiovascular disease, associating or not depression disease.

The second stage(Study of the relationship-atherosclerotic coronary artery disease-markers of inflammation, lactic acid-cognitive deficiency):

-The study of the relationship between depression and the markers of inflammation with lactic acid as a substrate of anxious depressive syndrome.

- -Studying the relationship of subclinical atherosclerosis-depression.
- -Studying the relationship between subclinical atherosclerosis-cognitive deficiency.

Objectives of the study:

Evaluation of depression in conjunction with cognitive status in patients with cardiovascular disease.

Evaluation of clinical-biological correlates depression-cognitive status in the geriatric patient.

Evaluation of Clinico-biological correlates Depression-lipid metabolism in the geriatric patient.

6.3 Study Protocol

6.3.1 Type of study and period of deployment

The study took place between January and June 2015 within the framework of the V-Medical Clinic, Iasi Railway Clinic Hospital.

The study was conducted on a number of 191 patients divided into four batches according to cardiovascular disease and the presence of depression or cognitive deficit.

6.3.2 Inclusion Criteria:

- 1. Men or women over 60 years of age.
- 2. Subjects who agree to the conditions of the study and sign informed consent.
- 3. Patients with clinical cardiovascular disease and the presence of depression or cognitive deficit.

6.3.3 Exclusion criteria:

- 1. Lack of agreement of the patient for participation in the study by signing informed consent;
- 2. Lack of patient adherence;
- 3. Subjects having historically chronic consumption of ethanol or illicit drugs;
- 4. Cognitive impairment or major psychotic disorders;
- 5. History of allergy to antihypertensive agents commonly used in clinical therapy, marked decrease in effort tolerability, Grade III or IV NYHA heart failure or history of decompensated cardiac failure;
- 6. Positive serological tests for hepatitis B, C and HIV that can influence hepatic metabolism and psychological status of people in the study;
- 7. Any affection that is decompensated.

Study group

The 191 subjects will be randomised to four equal batches:

- ➤ Group I: Normal Cognitive, comprising subjects cardiovascular disease andnormal psychological ageing, without cognitive deficiency or clinical depression-witness Group;
- ➤ Group II: Normal Cognitive, comprising subjects cardiovascular disease normal psychological ageing, without cognitive deficiency but with clinical depression;
- ➤ Group III: Dysfunctional cognitive disease, which included patients with clinically manifest cardiovascular illness and cognitive deficiency, mild or moderate, diagnosed according to DSM-IV or Petersen criteria;
- ➤ Group IV: Mixed psychopathology, which included patients with clinically manifest cardiovascular disease that have cognitive deficiency and depressed disorder at the same time.

6.3.4 Patient evaluation:

- -Inviting the patient to take part in this study and signing informed consent;
- -Recording of identity data;
- -Diagnosis
- -Personal history;
- -Heredo-Collateral history;
- -Socio-professional anamneosis;
- -Verification of vital parameters (TA, pulse, temperature);
- -Measurement of waist and weight;
- -EKG registration;
- -Laboratory examination (blood glucose, hemogram, TGP, TGO, cholesterol, urea, creatinine);
- -Evaluation of cognitive function through the MMSE screening tests (Mini-MentalState Examination 30 Itemi) depression by GDS (Geriatric Depression Scale-15 Itemi) tests.

6.3.5 Psychometric tools used

Hamilton Depression Rating Scale – HDRS

The HDRS scale introduced in 1960 by Hamilton is the most commonly used scale in the field, being an international instrument of communication between investigators. The scale is used in psycho pharmacological studies in a standard battery to assess the severity of symptoms and sensitivity to change. (Hamilton, 1960).

Hamilton Anxiety Rating Scale – HARS

The Hamilton Anxiety Rating Scale is one of the first instruments of quantification of anxieties and performed by Hamilton (1959) to quantify Anxiety Nevrozis. The scale achieves an evaluation of anxieties and identify symptoms of Natural, Psychic , and Somatic factors. The Geriatric Depression Scaleoes not miss a certain clinical nosology but detects symptoms of anxiety and assess their severity.(Hamilton, 2000)

MMSE(Mini-Mental State Examination)

MMSE is the most commonly known tool used in evaluating cognitive function. MMSE was drafted by Folstein in 1975. The maximum total value of score equal to 30 points indicates good cognitive performance. Studies have shown that dementia can be diagnosed with good accuracy in most situations at a score ranging from 24 to 27 points.

Geriatric Depression Scale-GDS

Scale of depression in geriatrics (yesavage et al.,1983) is the most commonly used scale in Elder psychiatry and has several versions, the short version being applied frequently. (Yaffe et al., 1999).

6.3.6 Statistical Processing

In the present study, the association between categories of events is essential for the research of causal relationships. Since the number of subjects is relatively low the samples are small, the distribution of the studied characteristics is normal. The data was uploaded and processed using the statistical functions of Microsoft Excell (Microsoft Corp.) and the statistical analysis package SPSS 17 (SPSS Inc.), a variant of statistical processing that allows the use of small batches of patients.

6.4 STUDY TAKES CLINICAL-BIOLOGICAL CORRELATES CARDIOVASCULAR RISK FACTORS DEPRESSION-COGNITIVE STATUS IN ELDERLY PATIENTS

6.4.1 Results

During the Group I observed statistically significant correlates between the presence of hypertension and cognitive status (p =-0.313, r = 0.028), respectively depression (p =-0.301, r = 0.036).

The presence of arterial hypertension correlated with low scores at MMSE and high scores at Hamilton Depression Rating Scale. MMSE scores have correlated backwards proportionately and statistically significantly with depression measured by both scales (R_{HRDS}=-0.453 p = 0.001 respectively R_{GDS}=-0.31 p = 0.03). Cognitive status and depression did not correlate significantly with the consumption of alcohol and smoking in the case of Group I (fig. 6.37) MMSE scores have correlated backwards proportionately and statistically significantly with depression measured by both scales (R_{HRDS}=-0.639 p \leq 0.001 respectively r_{GDS}= 0.291 p = 0.045). Cognitive status and depression did not correlate significantly with alcohol consumption and smoking in the case of Group II (fig. 6.38).

The presence of arterial hypertension correlated with high scores at Hamilton Depression Rating Scale. MMSE scores have correlated backwards proportionately and statistically significantly with depression measured by both scales (R_{HRDS} =-0.468 p = 0.001 respectively R_{GDS} =-0.373 p = 0.01). Cognitive status and depression did not correlate significantly with alcohol consumption and smoking in the case of Group III (fig. 6.39). MMSE scores have correlated backwards proportionately and statistically significantly with depression measured by both scales (R_{HRDS} =-0.463, p =0,001 respectively r_{GDS} =-0.516, p \leq 0.001).Cognitive status and depression did not correlate significantly with alcohol consumption and smoking in the case of Group IV (fig. 6.40).

Cognitive status (p =-0.338, r = 0.018) and depression (p _{HDRS}= 0.474, r = 0.001) were statistically significantly correlated with the determined values of uric acid (fig. 6.41).

Cognitive status (p =-0.342, r = 0.017) was statistically significantly correlated with the determined values of uric acid in the study Group II (fig. 6.42).

Cognitive status (p =-0.423, r = 0.003) was statistically significantly correlated with the determined values of uric acid in the case of Group III study (fig. 6.43).

No statistically significant correlation was recorded between cognitive status, depression, uric acid, urea, creatinine in the case of Group IV study (fig. 6.44).

Analisys correlation between cognitive status, depression and lipid metabolism has highlighted in the case of group and a statistically important relationship between elevated MMSE values and low cholesterol (p =-0.318, r = 0,026), triglycerides (p =-0.326, r = 0,022) and total cholesterol (p =-0.343, r = 0,016) (fig. 6.45).

Analisys of the correlation between cognitive status, depression and lipid metabolism revealed in the case of Group II a statistically important relationship between elevated MMSE values and low cholesterol levels (p = -0.420, r = 0.003) and total cholesterol (p = 0.372, r = 0.008) (fig. 6.46).

Analisys of the correlation between cognitive status, depression and lipid metabolism revealed in the case of Group III a statistically significant relationship between elevated MMSE values and low cholesterol (p =-0.438, r = 0.002), and total cholesterol (p =-0.449, r = 0.002) (fig. 6.47).

Analisys correlation between cognitive status, depression and lipid metabolism

revealed in the case of group IV a statistically important relationship between elevated MMSE values and low cholesterol (p =-0.506, r \leq 0.001), triglycerides (p = 0.399, r = 0.005) and total cholesterol (p =-0.758, r \leq 0.001) (fig. 6.48).

6.4.1.7. Regression analysis

Table LII sums the non-standard and standardised values of regression coefficients obtained for the model in which the cognitive status (MMSE) was dependent variable. In the model, there were introduced as independent variables uric acid, LDL-cholesterolul, triglycerides, total cholesterol respectively depression.

All these variables presented correlated over 0.30 with cognitive status (MMSE).

The resulting prediction pattern was statistically significant (R = 0509; $R^2_{adjusted} = 0.22$; $F_{47, 49} = 5.5$; P = 0.001), along with constant, independent variables taken into account explaining 50% of the variance of the score at MMSE.

Total cholesterol(β =-0.34; p = 0.023), depression (β =-0.34; p = 0.010), were negative PREDICTORS of MMSE. In other words, a high level of Cholesterol values and a more stressed degree of depression have tended to associate with a lower score at MMSE.

Table 6.LIII presents the non -standard and standardised values of regression coefficients obtained for the model in which the cognitive status (MMSE) was dependent variable. The model is used as independent variables uric acid, LDL-cholesterol, triglycerides, total cholesterol respectively depression. All these variables presented correlated over 0.30 with cognitive status (MMSE). The resulting prediction pattern was statistically significant (R = 0.71; $R^2_{adjusted} = 0.49$; $F_{45, 46} = 4.7$; p = 0034), along with constant, independent variables taken into account explaining 49.2% of the variance of the score at MMSE. The scores to depression measured both by the Hamilton scale (β =-0.65; $p \leq 0.001$), but and by the Geriatric Depression Scale- (β =-0.22; p = 0034), were negative predictors of MMSE.

In other words, a high level of depression has tended to associate with a lower score at MMSE. All these variables presented correlated over 0.30 with cognitive status (MMSE). The resulting prediction pattern was statistically significant (R = 0.72; $R^2_{adjusted} = 0.49$; $F_{47, 49} = 6.04$; p = 0.018), along with constant, independent variables taken into account explaining 50% of the variance of the score at MMSE.

Cholesterol Total (β =-0.40; p = 0.001), LDL-cholesterol (β =-0.36; p = 0.002), depression (β =-0.27; p = 0.018), were negative predictors of MMSE.

Table 6. LIV comprises the non-standard and standardised values of the regression coefficients obtained for the model in which the cognitive status (MMSE) was dependent variable. In the model, there were introduced as independent variables uric acid, LDL-cholesterol, triglycerides, total cholesterol respectively depression. In other words, a high level of total cholesterol levels, cholesterol and a more stressed degree of depression have tended to associate with a lower score at MMSE.

The resulting prediction pattern was statistically significant (R = 0.73; $R^2_{adjusted}$ = 0.71; F _{47, 49}= 10.6; p= 0.02), along with constant, independent variables taken into account explaining 50% of the variance of the score at MMSE. Total cholesterol (β =-0.52; p ≤ 0.001), LDL-cholesterol (β =-0.28; p = 0.002), depression (β =-0.35; p ≤ 0.018), were negative predictors of MMSE. In other words, a high level of total cholesterol levels, cholesterol and a more stressed degree of depression have tended to associate with a lower score at MMSE.

6.4.1.8 Discussions

Studies show that relationships between lipid metabolism and cerebral functions are complex exceeding the risk of vascular accident. A population observational study conducted

in 2 research centres over a period of 5 years on a number of 2632 subjects aged 74 years, advertised in 2004 followed the relationship syndrome Metabolic – Biological inflammatory syndrome (whichwas the determination of CRP and IL-6) – Modification of cognitive status (evaluated by MMSE). The evaluation of subjects was achieved at 3 and 5 years after inclusion for 1016 subjects with metabolic syndrome compared to 1616 subjects without metabolic syndrome, and It has been shown that the risk of cognitive deficiency is generally increased by approximately 20% in subjects with metabolic syndrome. The presence of inflammatory syndrome associated with metabolic syndrome increases the risk of cognitive decline to 66% to 4 years; Therefore, the inflammatory syndrome associates or does not allow a stratification of risk the cognitive decline in subjects with metabolic syndrome.

The results of studies of the relationship of metabolic syndrome with cognitive deficiency are similar to older observations that demonstrated that arterial hypertension and elevated serum cholesterol levels in the middle-aged population, either isolated or In the association, the risk increases at an advanced age to develop Alzheimer's disease. Analysis oftheir last year's studies emphasizes numerous interference between the risk factors of Alzheimer's dementia and vascular dementia, some of which are components of metabolic syndrome and pathogenic physio conditions associated with itsuch as: hypercholesterolemia, HTA, diabetes mellitus, increased resistance to insulin – which favours the activity of G-secretase, endothelial dysfunction – which occurs early in boala Alzheimer's. In particular an incomplete relationship is the one between diabetes mellitus and the presence ApoE4 increase the risk of Alzheimer's dementia and which correlates with Increased amounts of amiloid plaque and neurofibriulation degeneration.

The presence of amnesia disorders does not influence the response to treatment and the evolution of geriatric depression (Mattis et al. 1967). The impairment of these functions has not been associated with the presence of residual symptoms, relapses or recursions; There was even a reverse relationship between scores of amnesia evidence and the evolution of depressive symptoms during maintenance treatment (Angelopoulos et al.2009th). Executive dysfunctions in elderly depression have been associated with a weak response to antidepressant treatment, with increased risk of relapse and recusal and with the presence of residual depressive symptoms (Angelopoulos et al. 2009).

In the case of mild cognitive impairment, the initial form of cognitive deterioration, the MMSE screening test has a low sensitivity-49% but a large specificity of about 92%, so that patients with a score below 27 points already have a deficit Early cognitive or develop over time a dementia syndrome. The health report achieved at the request of the World Bank showed that cardiovascular diseases are the cause of mortality in about 30% of patients at the present time.

If it is sometimes easy to achieve the target level for a risk factor such as systolic blood pressure in the elderly patient, the total cardiovascular risk may be diminished by acting on risk factors such as smoking or cholesterol levels. The atherosclerosis process can be analyzed by non-invasive methods such as carotid Doppler ultrasound (IMT > 0.9 mm) that finds the process of early atherosclerosis and ankle-arm index (< 0.9) for the certification of evolved atherosclerosis. The carotid Doppler ultrasound quantifies the process of atherosclerosis specifically at the level of the common carotid arteries, during which, in general, other vascular areas such as the bifurcation of the common carotid arteries or internal carotid arteries are attacked of atherosclerosis.

The appearance of the atheromatous plaque is highlighted by an IMT > 1.3-1.5 mm or by increasing the thickness of 0.5 mm or with 50% of the surrounding IMT. In the analyses carried out, conducting Doppler ultrasound in untreated hypertensive patients without touching the target organs showed the presence of vascular disease, contributing to better stratification of the risk. In addition to the mechanical effect of shrinking the arterial lumen,

atheroma plates are also the place of training and use of a thrombus through the system instability of the plaque with cracking and breaking it especially in the case of old calcified and rigid plates, and from the cause of endothelial dysfunction with the decrease in nitric oxide secretion, resulting in decreased local vascular tone and increased thromboclastic aggregation and adhesion, and may occur acute ischemia and myocardial infarction or accident Stroke. The latest studies have revealed a new concept, i.e. "Early vascular Aging" EVA (Early Vascular Aging) – Reflecting the early development of the atherosclerosis process. EVA syndrome exhibits elevated arterial stiffness (atherosclerosis, PWV pulse wave velocity > 12 m/s), lifting central pulse pressure and/or brachial, atherosclerosis (IMT), endothelimal dysfunction, increased peripheral vascular resistance, Local and perivascular inflammation, increased oxidative stress, but the conditions of occurrence are attested by early biological ageing and insulin resistance with deviations and metabolic changes, abdominal obesity, chronic inflammation, Albuminuria, abnormal magnification pattern in the antenatal period.

Atherosclerosis, the substrate of cardiovascular disease, occurs and evolves through the combined activity of the risk elements, and their association has a multiplicative effect. The World Health Organisation's expectations show that coronary artery disease will remain an important cause of death for the next 20 years, accounting for 12.2% of overall mortality, overcoming mortality due to cancer, events HIV/AIDS or liver disease.

Consequently, the estimation of the process of systemic atherosclerosis by noninvasive methods such as carotid Doppler ultrasound by measuring the average intimate thickness plays a role of great importance in detecting high-risk patients. The application of primary prevention measures and their admission to the completion of revascularisation procedures result in the reduction of cardiovascular morbidity or mortality and the increase in life expectancy. The realization of the carotid Doppler ultrasound plays the role of the patients at increased risk of developing cardiovascular cases and ischemic stroke, and gives us an indication of atherosclerosis as a whole, resulting in a risk Cardiovascular increased. It has been shown that 17% of patients under 20 years old already have atherosclerosis lesions, which in those over 50 years of age are found in a percentage of more than 85% of cases, despite the fact that they are not yet clinically manifested. However Das et al.(2006,), with the help of an MRI of 2040 subjects, concluded that 11% of the seemingly healthy patients had a silent ischemic stroke. 84% of the participants had a single stroke, and 16% were Diagnosed with even more silent brain attacks. 52% of myocardial infarction occurred in basal ganglia, 35% in subcortical formations, and 11% in cortical areas.

6.4.1.9. Conclusions

- ➤ The association between cardiovascular disease-depression cognitive deficiency has been validated by highlighting statistically significant correlations between these nosologists in the case of the witness batch.
- ➤ The study did not reveal statistically significant differences according to gender between biochemical parameters studied neither in the case of the witness batch nor in the case of their batches presenting psychiatric pathology.
- ➤ The study of depression and mnesic function showed slightly higher levels in women without any statistically significant differences.
- ➤ The prevalence of severe amnesic disorders was higher in the case of the batch that associated cardiovascular disease depression and cognitive deficiency.
- The forms of severe dementia were identified in the Group that associated cardiovascular disease depression and cognitive deficit equal to both sexes the minimum score of the assigned MMSE was 10, the value attributed to forms of

- cognitive dysfunction severe.
- ➤ In the witness group, statistically significant correlates were observed between the presence of hypertension and scores on the instruments assessing the cognitive status or depression.
- > Smoking and alcohol consumption have not been associated with changes in cognitive status and depression in the overall study Group.
- ➤ The presence of arterial hypertension was associated with lower scores at MMSE and high scores at Hamilton Depression Rating Scale.
- ➤ MMSE scores were associated inversely proportionately and statistically significantly with the depression measured by both scales.
- In the Group III (patients with cardiovascular disease and depression) No statistically significant correlates between the presence of hypertension and cognitive status were observed but significant correlates with Depression.
- A significant combination of lipid metabolism and depression fractions and changes in cognitive functionhave been observed in the overall batch of study.
- ➤ The regression analysis of the overall study Group was that high level of total cholesterol levels, cholesterol and a higher degree of depression tended to associate with a lower score at MMSE.
- ➤ The study of liver damage in our research was based on a minimum of laboratory investigations, namely the determination of AST, ALT and GGT, complementing the hepatic ultrasound examination.
- ➤ The incidence of hepatic impairment was 7%, and was more frequently highlighted in the elderly compared to adults (13% vs. 4%), and in men versus women (3.3% vs. 1.2%). It follows that the relative risk of developing a liver injury is higher in men and in the elderly (LR = 1.18 vs. 1.01).
- ➤ The existence of statistically and strong significant correlation between the presence of alcohol and depression, and hepatic steatosis, demonstrates the need for minimal investigation of liver function in patients with depression.
- ➤ The determination of transaminases has proven to be an important predictor of depression. Consumption of alcohol has been shown to be the central element in both the development of depression and hepatic steatosis.

6.5. STUDY IB STUDY OF THE RELATIONSHIP-ATHEROSCLEROTIC CORONARY ARTERY DISEASE-MARKERS OF INFLAMMATION, LACTIC ACID-COGNITIVE DEFICIENCY

6.5.1. Premises of the study

Depression is an independent cardiovascular risk factor for possible coronary events in healthy appearance subjects. The association of anxiety and fear states with somatic diseases is a very well known fact. A percentage of 2.5% of psychiatric, outpatient or hospitalized patients simultaneously suffer from a somatic condition that is accompanied by anxious symptoms.

The asociation of the most known of anxious symptoms and somatic symptoms occurs in cardiovascular and respiratory diseases, which repeatedly cause states of fear, restlessness and anxious expectation. The fear of the presence of severe diseases, is exacerbated by the awareness of cardiac dysfunction (tachycardia, extrasystoles, rhymia), the occurrence of retrosternal pain, shortness of breath or sensation of physical exhaustion. This clinical evidence demonstrates the therapeutic combination of specific medication with mild

sedatives, recommended in the psychiatric clinic patients with primary anxiety disorders (not related to a somatic condition or other mental illness).

Between the mechanisms that show the relationship between depression and coronary artery disease are mentioned the correlations of depression with the expression of inflammatory indicators involved in the pathogenesis of atherosclerotic coronary artery disease. In the case of atherosclerotic coronary artery disease biological data confirms high serum levels of C-reactive protein and cytokine in depressed coronary artery patients. Concurrently C-reactive protein and proinflammatory cytokines actively facilitate behavioural changes that legitimate the depressed mood associated with coronary artery disease. Proinflammatory cytokines stimulate liver cells that synthesize C-reactive protein, thus said, its occurrence is a response to the presence of inflammation and tissue lesion.

6.5.2. Purpose of the study

Is to investigate fibrinogen interaction, C-reactive protein as an expression of inflammation and lactic acid as a substrate of depressive disease on the one hand and the relationship between subclinical atherosclerosis (measured indirectly) and these markers and cognitive deficit. The study aims to explore whether the determination of the C-reactive protein values of lactic acid and subclinical atherosclerosis have a predictive role in the occurrence of anxious-depressive events and cognitive deficit in coronary patients.

All patients had free consent to collaborate in the study, after explaining their purpose and duration of the study.

6.5.3. Objectives of the study:

Evaluation of depression and anxiety in conjunction with the inflammatory profile in patients with cardiovascular disease. Evaluation of clinical-biological correlates depression-anxiety-subclinical atherosclerosis in the geriatric patient.

6.5.4. Results

The study of the correlation between markers of subclinical atherosclerosis and cognitive status, depression and anxiety in the patients of Group I revealed the following significant correlations:

- **Fibrinogen** has been significantly correlated with lactic acid (P = 0357, r = 0,012), MMSE (p =-0.71, r \leq 0.001), Hamilton Anxiety Rating Scale p = 0.283, r = 0,049), Hamilton Depression Rating Scale (p = 0,386, r = 0,006), Geriatric Depression Scale (p = 0,309, r = 0,031), IGB (p = 0,529, r \leq 0.001), GIN (p = 0.623, r \leq 0.001).
- **CRP** has been significantly correlated with lactic acid (p =-0.05, r \leq 0.001), MMSE (p = 0.392, r = 0.005), Hamilton Anxiety Rating Scale (P = 0.492, r \leq 0.001), Hamilton Depression Rating Scale (p = 0.49, r \leq 0.001).
- **Lactic acid** correlated significantly CRP (p =-0.5, r \leq 0.001), fibrinogen (p = 0,357, r = 0,012) MMSE (p =-0.49, r \leq 0.001), Hamilton Depression Rating Scale (P = 0.792, r \leq 0.001), Hamilton Anxiety Rating Scale (p = 0.439, r \leq 0.001), Geriatric Depression Scale (p = 0.372, r = 0,008), GIM (p = 0.368, r = 0,009) (Fig. 6.73).

The study of the correlation between markers of subclinical atherosclerosis and cognitive status, depression and anxiety in the patients of the Group ii revealed the following significant correlations:

- **Fibrinogen** correlated significantly with, MMSE (p = 0.521, $r \le 0.001$), Hamilton Anxiety Rating Scale (P = 0.286, r = 0.046), Hamilton Depression Rating Scale (p = 0.357, r = 0.046)

- 0.012), CRP (p =-0.49, r ≤ 0.001)
- **CRP** has been significantly correlated with lactic acid (p =-0.48, r \leq 0.001), MMSE (p = 0.75, r \leq 0.001), Hamilton Anxiety Rating Scale (p =-0.349, r = 0.014), Hamilton Depression Rating Scale (p =-0.48, r \leq 0.001).
- **Lactic acid** was correlated with crp (P =-0.48, $r \le 0.001$), MMSE (p =-0.45, r = 0.001), Hamilton Anxiety Rating Scale (P = 0.595, $r \le 0.001$), Hamilton Depression Rating Scale (p= 0.44, $r \le 0.001$), Geriatric Depression Scale (p = 0.296, r = 0.039), GIM(p =-0.28, r = 0.046)(Fig. 6.74).

The study of the correlation between markers of subclinical atherosclerosis and cognitive status, depression and anxiety in the patients of Group III revealed the following significant correlations:

- **Fibrinogen**has been significantly correlated with MMSE (p =-0.58, r \leq 0.001), Hamilton Depression Rating Scale (P = 0.4, r = 0.005), Hamilton Anxiety Rating Scale (P = 0.331, r = 0.023), Geriatric Depression Scale (p = 0.48, r = 0.001), IGB (p = 0.64, r \leq 0.001), GIN (p = 0.56, r \leq 0.001) CRP (p =-0.35, r = 0.016).
- **CRP** has been significantly correlated with lactic acid (p =-0.55, r \leq 0.001), MMSE (p = 0.73, r \leq 0.001), Hamilton Depression Rating Scale (p =-0.4, R = 0.005), Hamilton Anxiety Rating Scale (p =-0.266, r = 0.07), Geriatric Depression Scale (p =-0.38, r = 0.008) =), IGB (p = 0.59, r \leq 0.001), GIM (p =-0.67, r \leq 0.001).
- **Lactic acid** correlated significantly CRP (p =-0.55, r \leq 0.001), MMSE (p =-0.43, r \leq 0.001), Hamilton Depression Rating Scale (p = 0.44, r \leq 0.001), Hamilton Anxiety Rating Scale (P = 0.546, r \leq 0.001), Geriatric Depression Scale(p = 0.44, r \leq 0.001), IGB (p = 0.45, r = 0.001), GIM (p = 0.54, r \leq 0.001) (Fig. 6.75).

The study of the correlation between markers of subclinical atherosclerosis and cognitive status, depression and anxiety in patients of Group IV revealed the following significant correlations:

- **Fibrinogen** significantly correlated MMSE (p =-0.48, r \leq 0.001), Hamilton Depression Rating Scale (P = 0.4, r = 0.05), Hamilton Anxiety Rating Scale (P = 0,331, r = 0,023), Geriatric Depression Scale (p = 0,48, r = 0.001), IGB (p = 0.64, r \leq 0.001), GIM (p = 0.56, r \leq 0.001) CRP (P =-0.35, r = 0.016).
- **CRP** has been significantly correlated with lactic acid (p =-0.55, r \leq 0.001), MMSE (p = 0.73, r \leq 0.001), Hamilton Depression Rating Scale (p =-0.4, r \leq 0.001), Hamilton Anxiety Rating Scale (p =-0.266, r = 0.07), Geriatric Depression Scale (p =-0.38, r = 0.008) =), IGB (p =-, 59, R \leq 0.001), GIM (p =-0.67, r \leq 0.001).
- **Lactic acid** correlated significantly CRP (p =-0.45, r \leq 0.001), MMSE (p =-0.53, r \leq 0.001), Hamilton Depression Rating Scale (p = 0.64, r \leq 0.001), Hamilton Anxiety Rating Scale (P = 0.546, r \leq 0.001), Geriatric Depression Scale (p = 0.64, r \leq 0.001), IGB (p = 0.45, r = 0.001), GIM (p = 0.4, r \leq 0.001) (Fig. 6.7)

6.5.4.4. Discussions

In degenerative processes specific to cardiovascular ageing, but also in cardiovascular diseases such as essential hypertension, structural and functional modifications of adaptive both at the vascular and microvascular level occur. The increase in the thickness of the intimate complex-mean carotid and the rarefaction of conjunctithe microcirculation (phenomenon characterized by a decrease in the density of arterioles and capillaries) are examples of such changes.

The thickness of the intimate-medium carotid complex can be used as a predictive index of subsequent cardiovascular and cerebrovascular events. It was confirmed that the thickness of the intimate complex-mean with cerebrovascular diseases, with symptomatic

cerebral infarction but also with cerebral lacunarism, and some researchers observed an association with asymmetric vascular Cerebro pathology, respectively with the left side of the brain. Hypertension has also been described as an independent risk factor, predictor of cerebral lacunarism and lesions of the white brain substance, viewed by nuclear magnetic resonance as gaps ("Lacuna"), respectively hyperintensities ("WMI"), which in turn are prognostic factors for the development over time of some cognitive deficits.

The number of evidence presenting the role of vascular component in the evolution of the Alzheimer's BowlII is continuously increasing; the very early hypofusions of the cerebral parenchymas lead to neuronal and cognitive deficits (Benarroch, 2007). It is appreciated in this way the identification of molecules with complex, parenchyatous and vascular activities. A number of substances have been experienced for the purpose of decreasing the vascular factor in Alzheimer's disease, with promising results: galantamine-acetylcholinesterase inhibitor that modulates and central nicotinic receptors for increasing transmission Cholinergic (Auchus et al, 2007); Memantine-Non-competitive antagonist with relative affinity of NMDA receptor, used to reduce glutamate-induced neurotoxicity (Molinuevo et al., 2000). The AVC is a case of increased risk for dementia and cognitive decline. According to DSM-IV, vascular dementia is diagnosed by the emergence and development of multiple cognitive deficits that cause memory disturbances and at least one of the following cognitive problems: Aphasia, Apraxia, agnosia and disruption in the functioning of Executive, with the emergence of focal neurological signs and symptoms indicating cerebrovascular disease, anomalies should not occur only during an episode of Delirium. In other news, according to the NINDAS-Airen criteria, to put the diagnosis of post-stroke dementia, the patient must be dementia, with clinical or radiological evidence of cerebrovascular disease, and the two can be correlated. Even if the exact data are missing due to the deficient definition of the disease, the use of different tools and difficulties in diagnosis to assess between the types of poststroke dementia and other cases of dementia, the post vascular accident is Appreciated the second type of dementia as a frequency. Since the research conducted so far has used different tools for the diagnosis of post-accident dementia and different methodologies in conducting the study, the incidence differs in studies between 8-30%. Silent brain scans shown on computer tomography could not predict the evolution of post-vascular accident dementia in a prospective experiment, but identifying on the MRI of some white substance tumors were associated with impaired cognitive function.

Obesity, insulin resistance and diabetes mellitus are known to be associated with increased mortality throughout the world. Patients with depression, anxiety or psychosis develop an increased risk of mortality for cardiovascular reasons compared to the general population due, in particular, to the fact that many antipsychotics and antidepressants facilitate growth in Weight (Viţalaru, 2010). Tricyclic antidepressants lead to the installation of insulin resistance and increase in plasma lipid levels fora no connection to the weight effect. At the same time, treatment with antidepressants like amitriptyline or doxepine lead to significant increase in body weight, which is mainly responsible for non-compliance with treatment. Are recently emerging antidepressant drugs, as serotonin reuptake inhibitors, which induce in the first phase a slight decrease in body weight but, long-lasting treatment with this model of medicines also lead to increased weight Body.

In female patients with major depression, abdominal adiposity was demonstrated using magnetic resonance tomography, showing increased visceral adiposity in situations with major depressive disorders. Serum concentrations between interleukin – 6-tumour necrosis factor Alfa are significantly increased in the Depression Group. The scarf of women presenting an increase in abdominal obesity may constitute a risk batch for the development of noninsulinodependent diabetes mellitus and metabolic syndrome. The results of this study lead to the assumption that immune and endocrine changes along with major depressive

disorders can lead to pathophysiological processes along with non-insulionodependent diabetes mellitus. An accomplished experiment followed the interference between marriage, depression and metabolic syndrome, assuming that depression has an intermediate role towards the development of metabolic syndrome, starting from some psychosocial factors. Therefore, the usefulness of lipid and glucose profile assessment is concluded, both at the beginning of an antidepressant treatment, but also during treatment. The treatment of hypertension in patients with depression should have angiotensin converting enzyme inhibitors, by their effect of cardiovascular protection. At the same time, physical exercise with positive repercussions on body weight, blood pressure and diabetes mellitus should be part of the therapeutic method of patients with depression.

Tricyclic antidepressants and monoamine oxidase inhibitors, to the same extent, decrease but also increase the levels of blood pressure (Viţalaru, 2010). Elevated levels of thiramine and increased noradrenaline release in sympathetic neurons have been detected in hypertensives following the administration of mono-oxidase inhibitors.

The territorial growth of noradrenergic cardiac activity can be the condition by which desipramine (a possible noradrenaline reuptake inhibitor) leads to increased blood pressure levels (Viţalaru, 2010). Another theory demonstrates that the central serotonergic system would be responsible for regulating blood pressure. Inhibition of serotonin uptake could cause a cascade of changes in the central neurotransmitting, with the emphasis on the tone of the vegetative nervous system. It was thus shown that fluoxetine and sertraline lead to the increase and stabilization of tension levels in patients with central hypotension and can be successfully used in the treatment of recurrence of hypotension. Regarding the clinical trial, orthostatic hypotension determined by treatment with tricyclic antidepressants is a negative repercussion of blood pressure increased, which was also recorded during treatment with monoamine oxidase inhibitors.

6.5.4.5. Conclusions

- In the control Group (patients presenting only cardiovascular disease) there were statistically significant correlates between the markers of inflammation, lactic acid subclinical atherosclerosis and the evaluation of depression and cognitive deficiency
- No statistically significant differences were shown in the overall study Group between the values of the parameters studied according to the sex of the patient.
- The markers of inflammation were statistically significantly correlated with scores when assessing depression (through both scales used) anxiety and evaluation of cognitive function
- Lactic acid as a substrate of anxiety correlated with depression and cognitive status
- ➤ IGB and GIM as indirect determinants of subclinical atherosclerosis have correlated with statistically significant both with depression and cognitive deficit.
- Regression analysis revealed that good predictors for the evolution of cognitive function of both lactic acid and GIM and IGB values. In other said elevated levels of lactic acid and GIM and IGB predict a more severe cognitive deterioration.

CHAPTER VII

STUDY II THE ADJUVANT ROLE OF NATURAL ANTIOXIDANTS IN THE THERAPY OF MEDIUM AND MILD COGNITIVE DYSFUNCTION.

7.1 Study Prestakes

The importance of oxidative stress in the production of Alzheimer's disease is demonstrated by numerous studies. Oxidative stress precedes the appearance of filaments of neurofibations and senile, patognomonic plates for this disease. It is not known exactly how oxidative stress is triggered, but the mechanisms involved are related to reduce reactions involving metals such as iron and copper (Perry, Cash, Smith, 2002).

The definition of oxidative stress has been revised over the past decades, now being considered an imbalance between pro-oxidant and antioxidant reactions, with two consequences: the occurrence of macromolecular lesions and/or interruption of signalling and Redox biological control. Redox reactions require electron transfer: the loss of one or more electrons by a donor is called oxidation and that substance, reducer, and the acceptance of electrons is called reduction and the substance that accepts, oxidizing. For the preservation of matter, these reactions are carried out at the same time, so that when a substance oxidizes, another is reduced. A defect in this chain of reactions causes oxidative stress, due to the fact that life is carried out in an aerob environment, where products containing carbon, hydrogen, nitrogen and sulphur are oxi, while oxygen serves as an electron acceptor, being finally reduced to water. (Jones, 2006, Ross et al, 2014)

7.2 Material and method

The research included 31 patients with mild cognitive disorder recruited from the patients of a private psychiatric clinic in the period from 1 June to 30 August 2014 divided into two batches. The Group I included 15 patients in specific treatment with antidementia medication and capsules with Catina oil (900mg), and Group II (control Group) included 16 patients with specific treatment with antidementia medication. Assessment of clinical and Paraclinic parameters and oxidative status achieved for each patient prior to inclusion in the study and after 6 months. Assessments were conducted: patients history and paraclinic evaluation included: determination of arterial pressure, heart rate, MMSE score and SOD dosing.

Inclusion Criteria of subjects were:

- -known amnesia disease with mild and moderate cognitive deficiency (MMSE 25-20)
- -consent of patients to participate in the study.

The exclusion criteria were represented

- absent amnesia disease
- -Refusal of patients to participate in the study

The MMSE test is the most commonly known tool used to evaluate cognitive function. MMSE was drafted by Folstein in 1975 to assess the cognition of psychiatric patients.

Superoxide dismutase is a family of antioxidant metalloenzymes involved in the defense system against reactive oxygen species. It converts superoxide radicals into water and hydrogen peroxide, which is then catalyzed in O2 and H2O by glutathione peroxidase and Catalaza. A special kit for the determination of superoxide dismutase was used for dosing.

All subjects included in the study were verbally informed of the purpose of the study in the form of their consent. The processing of statistical data was carried out with the SPSS 19.00 Program for Windows, establishing a threshold of significance statistics of $p \le 0.05$.

7.3 Results

The results of the comparative analysis of cognitive status and oxidative status in the two batches 6 months after the beginning of the study showed that there were statistically significant differences p < 0.05 for both the average Scores at MMSE, as well as the average of SOD values. (Table 8. II). Increased values highlighting in the case of Group I, Group of which has been administered and capsules Catina oil. The slight increases in MMSE have also been observed in the second batch, which are explainable by the intrinsic effect of antidementia medication, the SOD increases can be explained by the antioxidant effect of the Ginko Biloba extracts that are part of the standard Treatment of dementia to the vast majority of patients.

7.4 Discussions

Although researchers have begun to study the presence of free radicals for decades and their role in various conditions, cardiologists study the effects of free radicals only in the years 1970. Research gained importance in 1969 when the radical superoxide dismutanse was discovered. SOD has a role in the dismutation of the superoxidic radical. Any change in the balance of reactive species-antioxidants in the free radicals leads to an acceleration of oxidative strest by initiating cellular changes that then evolve towards cardiomopathias and heart failure. Information on the role of free radicals in cardiovascular diseases is close to the point where new therapies will not neglect the role of antioxidants. The essential molecule oxygen, sits at the base of energy metabolism and is involved in many degenerative conditions. In these conditions a role has low oxygen forms, known as reactive oxygen species, which are small, organic or anorganic molecules: singlet oxygen, hydrogen peroxide, anise superoxide, alkoxy and peroxy radicals, radical Hydroxyl, etc. These molecules are highly reactive by the presence of unpaired electrals and have in physiological conditions, important roles in normal metabolic processes (Leopold, Loscalzo, 2009).

In conditions of excessive temperatures, ultraviolet radiation, various pollutants, the level of reactive oxygen species increases, resulting in lesions at the cellular level. Reactive oxygen species occur in particular under the action of ionizing radiation. The effects of oxidative stress are accelerating in the presence of nitrosative stress, by the formation of reactive nitrogen species. There are antimicrobial molecules, reactive nitrogen species are derived from superoxide and nitric oxide. Peroxyinitrite is very reactive and reacts with various cellular components. (Hopps et al., 2009, Youngl, McEneny, 2001). Reactions of reactive oxygen species with cellular substrates are complex. The cause of oxidative lesions that causes apotheosis is not always evident.

Oxidative stress and inflammation are related to the evolution of cardiovascular diseases and acute coronary syndroms. Oxidative stress is an important element at all stages of the physiopathology of atherosclerosis and acute thrombotic episodes, including dyslipidemia endothelial dysfunction, myocardial ischemic damage, recurrent thrombosis, oxidation LDL. Oxidative stress has an important role in endothelial dysfunction in the picture of cardiovascular disease. Clinical trials and Pharmacovigilance reports that oxidative stress plays an extremely important role in cardiovascular abnormalities in different conditions and antioxidant therapy can have beneficial effects. Studies conducted on the heart showed that its exposureto free radicals leads tomodificationcontracting function and may produce structural abnormalities. In Vivo studies have been conducted to highlight the role of catecholamines in stress-induced cardiovascular diseases. Studies have shown that cardiac dysfunction can be induced by CRIt's The production of free radicals initiated by the oxidation of catecholamines. Studying the role of free radicals in cardiac ischemic phenomena showed that it was mediated by the dysfunctions of transport Ca2 + in the sarcoplasmic reticulum.

In vivo and in vitro the tests that underwent the studies that have the role of demonstrating the role of free radicals in the pathology of cardiac insufficiency and cardiomopies. Concentrations of free radicals are reducedof non-enzyme and enzyatic antioxidants. The role of antioxidants is not to remove oxidizers, but to maintain a level that does not trigger the inflammatory waterfall.

Experimentally demonstrated that increased oxidative stress and status change in antioxidants leads to changes iron the structure and functionality of the heart. Studies conducted on patients with heart failure showed the role of antioxidants very clearly. Polyphenols help to avoid cellular lesions caused by reactive species. Inflammation is the cause of chronic conditions, including the aging process.

7.5 Conclusions

There was a significant improvement in the oxidative status by modifying the SOD values (p = 0.001) in the study Group compared to the witness Group.

There was a significant improvement in cognitive status by modifying the MMSE ($p \le 0.001$) values in the study Group face of the witness Group.

CHAPTER VIII

STUDY III MARITAL ADAPTATION IN THE TEXT OF DEPRESSION AND COGNITIVE DEFICIT IN THE ELDERLY PATIENT

8. 1.Prestakes of the study

The concept of *marital adaptation*, as well as the concepts related to it (for example: marital satisfaction, marital bliss, marital relationship quality), is one of the most frequently studied dependent variables in psychology Couple. The marital adaptation was defined as the degree of accommodating their husbands, one from the other (Locke and Wallace, 1967; apud Vogel, 1983).

Spanier (1976) defines marital adaptation by using concepts previously used in literature, such as: marital satisfaction and consensus, cohesion level and degree of expression of affection by the partners of the conjugal couple. Glenn (2010) argue that it is more useful to deviate the marital adaptation as a variable that influences the quality of the relationship not included among the factors of the concept, because adaptation is a concept that relates to the

relationship between spouses than to the feelings the spouses experience in the relationship.

To understand the *interpersonal effect of depression*, research has also focused on the couple's relationship with depressive people. Such an approach is necessary for three reasons: the occurrence of depression is accompanied by marital stress, difficulties in interpersonal relationships in the case of depressive can be more easily highlighted in the case of marital relationship and depression affects both partners of couple.

Marital stress and depression occur specifically for women, Brown and Harris in the study conducted in 1979 showed that the lack of a stable relationship is a factor of vulnerability of women for depression. The absence of a close relationship with the husband also associates with depression. In 1978, Weissman and Myers said that in the case of unfortunate marriages there were 25 times more likely that partners would develop depressive symptoms.

8. 2. Purpose and objectives of the study

8. 2.1. The purpose

- -Determination of the influence of depression and cognitive deficit of the elderly patient with cardiovascular disease on the adaptation of the torque relationship.
- -Establishing socio-demographic characteristics influencing the marital adaptability of couples.

8. 2.2. Objectives

The primary objective of this study is to conduct an analysis of adaptation to the relationship of torque, both from the perspective of the caregivers and the patient with cardiovascular disease with depression and/or cognitive deficiency.

Secondary objectives:

- -Evaluating the adaptation to the relationship of torque according to the psychological status and the degree of autonomy of the patient
- -Evaluation of adaptation to the relationship of torque according to religious beliefs and affective state.
- -Evaluating associated pathologies and individual patient autonomy in the context of the impact on marital adaptation

8. 2.3 General hypothesis

Depression and the patient's cognitive deficit influence the marital adaptation of both partners. Religious beliefs and affective state of both partners are influenced by the depression and cognitive deficit of the patient.

8. 2.3.1 Research Assumptions

- 1. The Group type influences the level of marital satisfaction, consensus, marital cohesion and diadic adaptation reported by patients/caregivers.
- 2. The Group type influences the religiousness, positive and negative affectiveness reported by patients/caregiver.
- 3. Religiousness and positive affectiveness positively correlate with the marital adaptation of patients within each Group.
- 4. Depression, cognitive deficit depression and negative affection of patients negatively correlate with the marital adaptation of the defenders within each Group.

8. 2.4 Groups of study

Those subjects will be randomised in three batches:

Group I: Subjects with cardiovascular disease, normal psychological ageing, and clinical depression.

- Group II: Subjects with cardiovascular disease and mild or moderate cognitive deficiency,
- Group III: Subjects with cardiovascular disease who have cognitive deficiency and depressed disorder at the same time;

8. 2.5 Evaluation of patients:

- -Inviting the patient to take part in this study and signing informed consent;
- -Recording of passport data;

Diagnosis

- -Pathological personal history
- -Socio-professional anamneosis;
- -EKG registration;
- -Evaluation of cognitive function through MMSE screening tests (Mini-MentalState Examination 30 Items) depression by GSD (Geriatric Depression Scale-15 Items) tests

8. 2.6. Inclusion criteria:

- 1. Men or women over 60 years of age.
- 2. Subjects who agree to the conditions of the study and sign informed consent.
- 3. Patients with cardiovascular disease presenting depression, cognitive deficiency or both.

8. 2.7. Exclusion criteria:

- 1. Lack of agreement of the patient for participation in the study by signing informed consent
- 2. Lack of patient compliance
- 3. Subjects having chronic consumption of ethanol or illicit drugs in history.
- 4. Major cognitive impairment or major psychotic disorders
- 7. Any cardiovascular, respiratory, neurological, renal, hepatic, endocrinological, haematological or immunological decompensated conditions.

8. 3. Material and Method

The study took place between July and October 2015 in a private clinic, the main purpose of which is the multidisciplinary approach of the psychiatric patient.

The study was conducted on a number of 72 couples, one of the partners being patient of the clinic.

The division into the three batches was performed according to the presence of cardiovascular disease, the depression of the cognitive deficiency.

The inclusion in the study was performed in the order of presentation in the clinic for the monthly consul.

8. 4. Psycho Metric tools used

MMSE (Mini-Mental State Examination)

The MMSE test is the most common tool used in evaluating cognitive function. MMSE was developed by Folstein in 1975 to assess cognitive status.

Scala of geriatric depression

The scala of geriatric depression (Geriatric Depression Scale, GSD-Yesavage et al. 1983) is a self-assessment tool with a simple format (YES/NO), which can be applied by an

evaluator without special training, so being easy to use.

It is the most common scale in elder psychiatry and has several versions, ranging from 30 to 15 Itemi, short version being applied more frequently (Yaffe et al., 1999).

The Revised dyadic Adjustment scale/RDAS was proposed by Dean M. Busby et aL. (1995), a version that includes only 14 of the 32 items of dyadic adjustment Scale/RDAS (Spanier, 1976).

Turliuc and Muraru (2013) adapted the RDAS, the coaches presenting convincing psychometric data, about the factorial structure, the psychometric properties of the items, the fidelity and the concurrent validity of The RDAS scale. The exploratory factorial analyses highlighted three factors that explained over 65% of the variance of scores at items, the factorial structure being supported by the data of the factorial analysis confirmatories.

Santa Clara Strength of religious faith Questionnaire (Plants & Boccaccini, 1997) measures personal religious belief, contains 10 items with variants of response from 1-strong disagreement to 4-strong accord.

List of positive and negative affects (PANAS, Watson, Clark, Tellegen, 1998b). The list of positive and negative diseases is a tool with 20 items (self-report type) that measures positive and negative affects.

PANAS reflects the dimensions of the negative provisions of type distress, while the AP represents engaging in pleasant experiences. The *positive* and *negative affects* label scores, according to the authors, the activation of positive and negative values of the affects. Respondents are asked to assess to what extent they lived, each of the twenty emotions specified, in the last month (the temporal framework referred to for the assessment of emotions varies, are studies in which the reporting is done at last week). The score of the two scales represents the arithmetic mean of the scores of the corresponding scale items.

8. 5. Statistical processing

The data was uploaded and processed using the statistical functions of Microsoft Excell (Microsoft Corp.) and the statistical analysis package SPSS 17 (SPSS Inc.), a variant of statistical processing that allows the use of small batches of patients.

8.6 Results

The correlation analysis of marital adaptation with cognitive deficit, patient depression revealed in the case of patients belonging to the group and statistically significant correlation between these parameters. Adaptation to the relationship of torque negatively correlates with geriatric depression (r = -0.49, p = 0.008). Negative affects were correlated with geriatric depression marital consensus (p = -0.5, p = 0.005). (Table 8.XL)

The correlation analysis of marital adaptation with cognitive deficit, patient depression revealed in the case of patients belonging to the Group II statistically significant correlation between these parameters. Adaptation to the relationship of torque negatively correlates with cognitive status (R =-0.54, p = 0,009). Negative affects were correlated with cognitive status and marital consensus (p =-0.53, r = 0,009) and cohesion (R =-0.49, p = 0.01) and marital satisfaction (R =-0.46, p = 0,027) (table 8.XLI).

The correlation analysis of marital adaptation with cognitive deficit, patient depression revealed in the case of patients belonging to Group III statistically significant correlation

between these parameters. Adaptation to the relationship of torque negatively correlates with cognitive status (r = -0.58 p = 0.005). Negative affects were correlated with cognitive status and marital consensus (p =-0.56, r = 0,007) and marital satisfaction (R =-0.58, p = 0.005). Geriatric depression negatively correlates with marital cohesion in patients of this group (R =-0.53, p = 0.01) (table 8.XLII).

The correlation analysis of marital adaptation with religious beliefs and the affective state of patients and the majority of the group and correlations revealed statistically significant correlations between the adaptation to the relationship of torque and beliefs (r = 0.49, p = 0.009), in positive affects (R = 0.47, p = 0.01) and negative affects (R = -0.43, p = 0.02), in the case of the caregiver.

Significant correlation of the scores of the defenders were also revealed in the case of marital satisfaction of positive affection (r=0.44, p=0=0.01) Negative affects (r=-0.44, p=0.01) and religious beliefs (r=0.44, p=0.02), marital cohesion and positive conditions (R=0.43, p=0.02) negative (r=-0.44, p=0.02) and religious beliefs (r=0.43, p=0.02 marital consensus and positive affects (R=0.05, P=0.007) negative affects (R=0.04), P=0.003) and religious beliefs (P=0.46), P=0.01). In the case of patients, the following correlates were determined:

Marital adaptation significantly correlates with the scale of religious beliefs (r=0.43, p=0.02) positive conditions (R=0.44, p=0.02) and with negative affects (R=0.48, p=0.01). Marital consensus correlates with positive affects (R=0.40, P=0.03) and negative affects (R=0.5, P=0.008) but also with religiosity (P=0.48, P=0.01). Marital satisfaction correlates with positive affects (P=0.48, P=0.01). Marital cohesion significantly correlates with negative affects (P=0.40, P=0.03) and religiosity (P=0.046, P=0.01) (table 8.XLIII).

The correlation analysis of marital adaptation with religious beliefs and the affective state of patients and the caregips of the Group II correlations revealed statistically significant correlations between adaptation to the relationship of couples and religious beliefs (r=0.46, p=0.02), positive affects (r=0.45, p=0.02) and negative affects (r=0.42, p=0.04), in the case of the caregiver. Other significant related correlates were: marital consensus-positive affects (r=0.48, p=0.01) and religiosity (r=0.46, p=0.02).

Marital Satisfaction-positive affectiveness (r = 0.46, p = 0.02) and religiosity (r = 0.5, p = 0.01)

Marital cohesion and negative affects (r = 0.05, p = 0.01)

In the case of patients, the following correlates were determined:

Marital adaptation significantly correlates with the scale of religious beliefs (r = 0.41, p = 0.03) Positive disorders (r = 0.49, p = 0.01) and negative affects (R = -0.05, p = 0.008).

Marital consensus-positive affects (r = 0.49, p = 0.01) and negative affects (R = -0.5, p = 0.003), religiosity (r = 0.41, p = 0.03).

Marital satisfaction-positive affects (R = 0.54, p = 0.001) and negative affects (R = 0.43, p = 0.03)

Marital cohesion-negative affects (R =-0.44, p = 0.02) and negative religiosity (R =-0.39, p = 0.04) (table 8.XliV).

The correlation analysis of marital adaptation with religious beliefs and the affective state of patients and the caregivers of the Group III correlations revealed statistically significant correlations between adaptation to the relationship of couples and religious beliefs (r = 0.49, p = 0.01), positive disorders (r = 0.45, p = 0.02) and negative affects (R = -0.49, p = 0.01), in the case of the caregiver. Other significant evidented correlates were:

Marital consensus-negative affectiveness (R =-0.5, p = 0.01) and religiosity (r = 0, 5, p = 0.01). Marital Satisfaction-positive affects (r = 0, 5, p = 0.01) and negative affects (R =-0.46, p = 0.02), religiosity (r = 0.5, p = 0.02). And positive affects (r = 0.45, p = 0.02) and negative affects (R =-0.42, p = 0.02), religiosity (r = 0.4, p = 0.04).

In the case of patients, the following correlates were determined

Marital adaptation significantly correlates with the scale of religious beliefs (p = 0,48, P = 0.02) positive affects (R = 0.44, p = 0.04) and negative affects (R =-0.5, p = 0.01). Marital consensus-positive affects (r = 0,53, p = 0.01). Marital Satisfaction-positive affects (r =-0.53, p = 0.01) and religiosity (r = 0.5, p = 0,007). Marital Cohesion-negative affects (R =-0.67, p = 0.001) and religiosity (r = 0.46, p = 0.03) (Table 8.XLV).

Data of multivariated linear regression analyses in Group I

Table 9. XLVI sums the non-standard and standardised values of regression coefficients obtained for the model in which the adaptation to the torque relationship was dependent variable in the case of patients belonging to the Group I. Also, for each of the independent variables, the unique contribution was calculated to explain the variance of the dependent variable (that the product between the semi-partial correlation value provided by the SPSS application and 100). In the model, the positive and negative affectiveness and religiosity were introduced as independent variables. All these variables presented correlates over 0.30 with marital adaptation. In addition, the variables that we have listed have shown correlated values below | 0.50 |, thus being ensured the avoidance of the multicolor of independent variables to be introduced into a prediction model.

The resulting prediction pattern was statistically significant (R = 0.47; $R^2_{adjusted}$ = 0.49; $F_{1.25}$ = 7.46; p < 0.001), along with constant, independent variables taken into account explaining 49% of the variance of the score to marital adaptation. Positive affectation (β = 0.30; p < 0.001), were positive predictors of marital adaptation in other words, a high level of positive affectation of the tins to associate with a higher score on marital adaptation. The independent variable explained 4.95% of the variance of the score adaptation to the torque relationship.

Table 9.XIVII The presents the non-standard and standardised values of regression coefficients obtained for the model in which adaptation to the torque relationship was dependent variable in patients belonging to Group I.

Also, for each of the independent variables, the unique contribution was calculated to explain the variance of the dependent variable (that the product between the semi-partial correlation value provided by the SPSS application and 100).

In the model, there were introduced as independent variables positive and negative affectiveness and religiousness, the degree of geriatric depression and the score to cognitive evaluation.

All these variables presented correlates over 0.30 with marital adaptation.

In addition, the variables that we have listed have shown correlated values below \mid 0.50 \mid , thus being ensured the avoidance of the multicolor of independent variables to be introduced into a prediction model.

The resulting prediction pattern was statistically significant (R = 0.66; $R^2_{adjusted}$ = 0.39; F _{1.25}= 9.46; p < 0.001), along with constant, independent variables taken into account explaining 39% of the variance of the score to marital adaptation. Negative affectation (β = 0.50; p < 0.001) and the degree of geriatric depression were negative predictors of marital adaptation.

In other words, a high level of negative affection and depression tended to associate with a lower score on marital adaptation. The two independent variables explained between 3.8% and 5.6% of the variance of the score adaptation to the couples relationship.

Data of multivariated linear regression analyses in Group II

Table 9. XLVI represents the non-standard and standardised values of the regression coefficients obtained for the model in which the adaptation to the torque relationship has been dependent variable in the case of patients 'caregivers belonging to the Group II.

Also, for each of the independent variables, the unique contribution was calculated to explain the variance of the dependent variable (that the product between the semi-partial correlation value provided by the SPSS application and 100).

In the model, the positive and negative affectiveness and religiosity were introduced as independent variables. All these variables presented correlates over 0.30 with marital adaptation.

In addition, the variables that we have listed have shown correlated values below \mid 0.50 \mid , thus being ensured the avoidance of the multicolor of independent variables to be introduced into a prediction model.

The resulting prediction pattern was statistically significant (R = 0.81; $R^2_{adjusted} = 0.61$; $F_{1.25} = 12.7$; p < 0.001), along with constant, independent variables taken into account explaining 49% of the variance of the score to marital adaptation.

Negative disorders (β =-0.23; p < 0.001) were negative predictors of marital adaptation. Religiousness was a positive predictor of marital adaptation (β =-0.25; p < 0.001).

A high level of negative affections of the tins to associate with a lower score on marital adaptation, while an increased religious score was associated with an increased score of the studied dependent variable.

Independent variables explained between 4.45 and 5.8% of the variance of the score adaptation to the couples relationship.

Table 9.Xl represents the non-standard and standardised values of the regression coefficients obtained for the model in which adaptation to the torque relationship was dependent variable in patients belonging to the Group II.

Also, for each of the independent variables, the unique contribution was calculated to explain the variance of the dependent variable (that the product between the semi-partial correlation value provided by the SPSS application and 100).

In the model, there were introduced as independent variables positive and negative affectiveness and religiousness, the degree of geriatric depression and the score to cognitive evaluation. All these variables presented correlates over 0.30 with marital adaptation.

In addition, the variables that we have listed have shown correlated values below $\mid 0.50 \mid$, thus being ensured the avoidance of the multicolor of independent variables to be introduced into a prediction model.

The resulting prediction pattern was statistically significant (R = 0.65; $R^2_{adjusted}$ = 0.47; $F_{1.25}$ = 7.67; p < 0.001), along with constant, independent variables taken into account explaining 47% of the variance of the score to marital adaptation. Negative disorders (β = 0.6; p < 0.001) and the degree of geriatric depression (β = 0.09; p < 0.001), were negative predictors of marital adjustment. In other words, a high level of negative affection and depression tended to associate with a lower score on marital adaptation. The two independent variables explained between 4.8% and 5.4% of the variance of the score adaptation to the couples relationship.

Data of multivariated linear regression analyses in Group III

Table 9.XII represents the non-standard and standardised values of the regression coefficients obtained for the model in which the adaptation to the torque relationship was dependent variable in the case of the patients belonging to the Group III.

Also, for each of the independent variables, the unique contribution was calculated to explain the variance of the dependent variable (that the product between the semi-partial

correlation value provided by the SPSS application and 100). In the model, the positive and negative affectiveness and religiosity were introduced as independent variables. All these variables presented correlates over 0.30 with marital adaptation. In addition, the variables that we have listed have shown correlated values below | 0.50 |, thus being ensured the avoidance of the multicolor of independent variables to be introduced into a prediction model.

The resulting prediction pattern was statistically significant (R = 0.71; $R^2_{adjusted}$ = 0.45; $F_{1.25}$ = 9.37; p < 0.001), along with constant, independent variables taken into account explaining 45% of the variance of the score to marital adaptation. Positive affectation (β = 0.38; p < 0.001), were positive predictors of marital adaptation in other words, a high level of positive affectation of the tins to associate with a higher score on marital adaptation. The independent variable explained 5.95% of the variance of the score adaptation to the torque relationship.

Table 9.LI presents the non-standard and standardised values of regression coefficients obtained for the model in which adaptation to the torque relationship was dependent variable in patients belonging to GROUP III. Also, for each of the independent variables, the unique contribution was calculated to explain the variance of the dependent variable (that the product between the semi-partial correlation value provided by the SPSS application and 100). In the model, there were introduced as independent variables positive and negative affectiveness and religiousness, the degree of geriatric depression and the score to cognitive evaluation.

All these variables presented correlates over 0.30 with marital adaptation. In addition, the variables that we have listed have shown correlated values below $\mid 0.50 \mid$, thus being ensured the avoidance of the multicolor of independent variables to be introduced into a prediction model. The resulting prediction pattern was statistically significant (R = 0.71; $R^2_{adjusted} = 0.45$; $F_{1.25} = 9.37$; $P_{1.25} = 9.37$;

Negative affectation (β =-0.60; p < 0.001), the degree of geriatric depression (β =-0.08; p < 0.001) and MMSE (β =-0.34; p < 0.001) were negative predictors of marital adaptation. In other words, a high level of negative affection, geriatric depression and a low level of cognitive evaluation tended to associate with a lower score on marital adaptation. The two independent variables explained between 4.6% and 4.8% of the variance of the score adaptation to the couples relationship.

8.7. Discussions

The results of this study should be analysed in the context of a study conducted on a relatively small number of subjects, consisting of married adults, neomogens in terms of ethnicity, religion, education, even heterogeneous viewers and marital status. Depression and cognitive status have proved to be factors affecting marital adaptation in all its aspects to all study batches.

The depression of one of the partners influences the cohesion of the couple and brings it to a standstill confirmed in numerous studies. Compared to happy married people, the married partners in stalemate are 3 times more likely to have a mood disorder, 2.5 times increased the chances of achieving an anxiety disorder, 2 times more likely to have a disorder to use of halluclogenic substances and 5.5 times increased the chances of reporting problems of domestic violence. Moreover, in couples in stalemate-especially negative communication-has direct adverse cardiovascular, endocrine, immune, neurosensory and other physiological systems that in turn contributes to physical health problems (Kiecolt, Newton, 2001). Despite the recognition and treatment of mood disorders, understanding the mechanisms of interpersonal context of depressive disorders remains a vital area of scientific research.

The theories that will address from an interpersonal perspective depression should take

better account of the epidemiology of depression and gender differences in depression, as well as the inclusion of ideas from other areas (Uzma et al., 2011). The full potential of theoretical and empirical advances that can be achieved by carefully detailing and investigating the spousal context of depression has not been addressed. In part, this is due to the methodological limitations of past research, especially the problems that arise because of the low selection sample. Also, much of these researches were developed in a theoretical vacuum, despite the availability of interpersonal models of depression. Traditionally, it was more challenging to test the reciprocal and dynamic patterns of association between contextual variables and depression, but methodological and statistical advances make this more feasible. The context of depression changes continuously and runs over time.

The correlation between depression and dysfunctional marital interaction is well documented, but only a few studies have examined gender-related differences in couples' conjugal interaction models with a depressed partner. Bodenmann analysed the differences in communication in married couples in a sample of 62 Swiss couples who present themselves for the treatment of depression. There were 16 stressed married couples, with a depressed wife, 21 married couples with a depressed wife, 18 stressed married couples, with a depressing husband and 7 unmarried couples with a depressed husband. The behavior of conjugal interaction was found to depend on sex, depression, marital stress, as well as the depressed partner type. The results suggest the need for a gender-sensitive model of the link between conjugal interaction and depression. Despite these concerns and limitations, in this study, different models of interaction were identified in couples with a depressed partner associated with the genus and suffering of married couples (Bodenmann, Meuwly, Kayser, 2011).

People with depression have as a main feature, the term adinamism, that they become incapable of realizing even the usual daily activities, alongside their closest ones. This can be judged totally erroneous by the life partner who has a normal physical and psychic tonus, can confuse as a kind of negative pronunciation of the depressive person, who does not make too much effort to get out of this state. The partner of the depressed one, can reach the situation where he will feel neglected or unloved, can realize that it has become pointless or that the relationship is about to end. Such feelings are natural if we consider that the closest person has an extremely different behavior without justified reasons, without being able to justify his state of mind, leaving the impression that he no longer needs anyone and nothing.

Based on romantic love, the perfect conjugal relationship emphasizes the mobility of roles, the sharing of responsibilities, the relationship having a compassionate aspect under its action both the woman and the man can be considered to be equal partners, Together, they also participate in the maintenance of the relationship and equally share the privileges resulting from the sense of bodily and psychological safety within the marriage. Under the influence of gender differences that have been assumed, there may be similarities to conceptualizing the genderized types of communication (Bem, 1975).

Women see men in speech just as they notice-more direct and more oriented towards the pursuit of pragmatic goals in communication. Typical aspects of men in communication, perceived by the feminine genre, but they do not consider them to be priority, represent the emphasis in the competition between them in communicating with others – the desire to expose knowledge, to show opinions On the topics of conversation. In the same way, men see female people in communication, in full, in the same way as women are observed: less direct in approach, more careful in sorting and using speech, directed towards achieving goals relational.

Remarkable was especially the idea that female individuals prefer as special behaviors in speech two types highlighted and from the point of view of men: focusing on details in communicating with others and excess verbalization (indiscretion, Gossip, nagging).

There are gender priority similarities in the composition and exposure of communication type. Even if we do not take into account gender, the exposures of the analyzed social subjects showed the importance of context (the communication framework, the level of intimacy of those who converse, personality types). At official areas, or in cases where the level of familiarity is reduced and women, and men, require a period of accommodation feeling pressures, constraints, using a formal conversation. A priority similarity is highlighted in the influence of professional training towards the kind of communication – the nature of professional preparation, where systematic interference with humans occurs, helps to form individual communicational skills, helping the individual to have a more elastic, disinhibited way that requires better accommodation capacity at various communicational situations (Hymes, 1972).

8.8. Conclusions

The average scores obtained by the subjects of the three batches in marital satisfaction, consensus, marital cohesion and diadic adaptation were statistically significantly higher in batches II and II compared to Group III.

The analysis of the differences in the averages of the three batches reported at the level of positive, negative and religious disorders reported by the caregivers revealed statistically significant differences in the values of the I Group and other study batches. Group I and Group II also had the values of the environments of the parameters you remember close.

The marital adaptation was statistically significantly correlated with cognitive deficit and depression in patients belonging to Group I.

Geriatric depression has negatively correlated with marital consensus, cohesion and marital satisfaction in all study batches.

The marital adaptation was statistically significantly correlated with cognitive deficit and depression in patients belonging to the Group II.

The marital adaptation was statistically significantly correlated with cognitive deficit and depression in patients belonging to Group III.

The cognitive status has negatively correlated with marital consensus and marital satisfaction, and geriatric depression correlates negatively with marital cohesion in the case of patients of this Group.

The cohesion and marital consensus with marital satisfaction has positively correlated with the positive and religious beliefs and the negative has correlated with negative conditions both in the case of the caregiver and patients in All three study batches.

Positive predictors for adaptation to the relationship of torque were the positive affectiveness for the caregiver of all three study batches, the peculiarity arises in the case of Group II where religiousness is also a positive predictor.

A high level of negative affectiveness of the tins to associate with a lower score on marital adaptation, while an increased religious score was associated with an increased score of marital adaptation in the case of Group II.

In the case of patients belonging to the three batches of study negative predictors for marital adaptation were negative disorders and the degree of geriatric depression, the patients of the Group III cumulated in addition to the two factors remember and the degree of cognitive deficiency as a negative predictor.

A high level of negative affects, geriatric depression and a low level of cognitive evaluation have tended to associate with a lower score on marital adaptation.

CHAPTER X

GENERAL CONCLUSIONS

The association between cardiovascular disease-depression – Cognitive deficiency is valid, the prevalence of severe medical disorders being high in patients who associate cardiovascular disease depression and cognitive deficit without differences in sex function.

The presence of arterial hypertension and dyslipidemia is associated with more pronounced cognitive deficiency and more severe forms of depression.

Statistically significant differences between the presence of alcohol, depression, and hepatic steatosis demonstrate the need for minimal investigation of liver function in patients with depression. Transaminases are an important predictor of depression, with alcohol being the central element both in the development of depression and hepatic steatosis.

Severe depression has as a substrate inflammation, which is proven by the increased values of its markers. In high serum lactic acid as a substrate of anxiety is associated with increased depression and impaired cognitive status.

The negative effect leads to a decrease in marital adaptation, while an increased score of religiosity stabilizes the marital torque by increasing marital adaptation.

Negative predictors for marital adaptation are negative disorders and the degree of geriatric depression, and patients cumulating in addition to the two factors you remember and a high degree of cognitive deficiency have extremely low marital cohesion.

All three components of the marital adaptation of cohesion, marital consensus and marital satisfaction are positively influenced by the positive affections and religious and negative beliefs of negative diseases both in and patients.

CHAPTER XI

ELEMENTS OF ORIGINALITY AND PERSPECTIVES THAT THE THESIS OPENS

The thesis debated a topical theme studied in the literature namely depression and cognitive deficiency in the patient with cardiovascular disease an important topic for clinical medicine, growing pathologies worldwide and implicitly in Romania. The present research includes one of the few studies addressing the multidimensional elderly patient, on the one hand, studies from a pathophysiological perspective the two pathologies mentioned above and frequently encountered in the elderly population, and on the other hand their consequences in their family life. Identify relationships between depression and cognitive dysfunction in thirdage people and establish the qualitative ratio of depression with decreased cognitive efficiency and their association with the presence of cardiovascular risk factors and implicitly of cardiovascular disease confirms the need to apply specific questionnaires to determine these conditions as a routine screening procedure in elderly people with cardiovascular disease. Early detection of depression in patients with cardiovascular disease and guidance to specific medical services, and following treatment in early phases, decreases the risk of developing memory disease.

Assessment of cardiovascular risk factors in conjunction with the assessment of subclinical atherosclerosis and the application of questionnaires for the determination of depression and cognitive deficit in patients at risk could be implemented in a programme of

monitoring of the elder. The advantages are on all plans: non-invasive maneuvers, low costs, the possibility of early diagnosis of cognitive decline and the establishment of treatment, which thus prevents or delays as much the need for institutionalization of these sick. In the case of a marital couple, there may be life events that cause unexpected crises, such as finding out the diagnosis of a chronic disease that one of the partners suffers, which significantly influences the marital adaptation of both partners, from here deriving the necessity of providing psychological support and not only to the marital partner not only the sick person. The most common reaction-related patterns in crisis situations may include both depressive and anxious symptoms and the possibility of more severe psychiatric imbalances, which include confusion in the cognitive plan, disorganization behaviour or problems in regulating strong negative emotions, the last mentioned situation is also highlighted in the present study. The work could open the prospect of interdisciplinary studies from the medical and psychological perspective, highlighting both the need for care of psychological support specialised for both the patient and the caregiving.

A limitation of our study is the relatively small number of participants and the fact that research took place only at the level of a medical centre in Iasi, which does not allow us to draw conclusions applicable to the entire population. The extension of the study Group on the number of subjects would confer a higher statistical power on the results and would also allow for the making of valid comparisons between batches by increasing the number of participants. Discussions on the possibility of conducting the screening of the elderly should remain open at the appropriate time to identify the risk factors for the two conditions by clinical methods.

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