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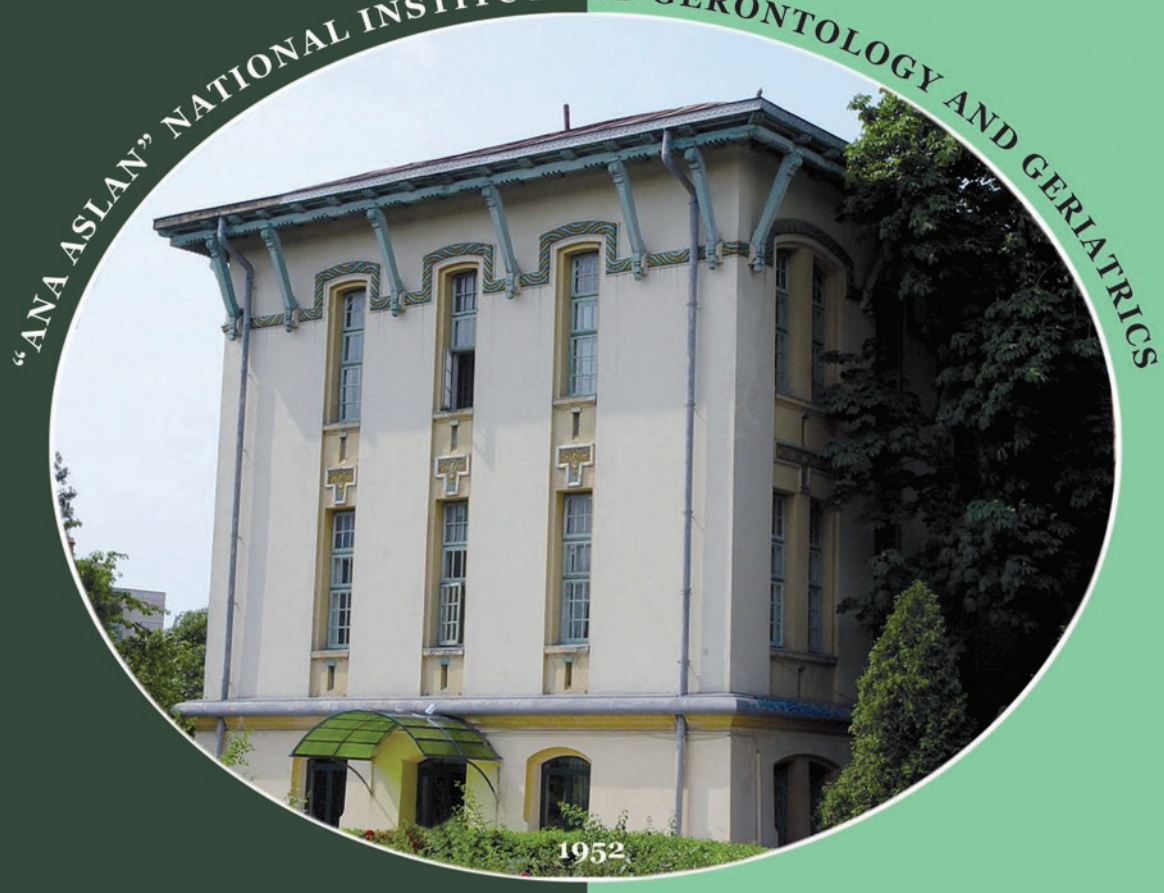

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OBSERVATIONS REGARDING A LONGEVOUS PATIENTS' GROUP OF THE NATIONAL INSTITUTE OF GERONTOLOGY AND GERIATRICS "ANA ASLAN"

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Abstract. Aim: To identify by a pluridisciplinary team (physicians geriatricians, biologists, biochemists, psychologists, sociologists) factors influencing human longevity which contribute to "optimal" and "successful" aging. The study-group until now included 135 subjects of which 115 aged between 85 and 89 years and 20 subjects aged 90 to 99 years. Regarding sex distribution there were 111 women and 24 men. Patient history consisted of collection of data about age, month of birth, inherited diseases, diet, marital status, fertility in women, age at first period and menopause, lifestyle, MMSE testing, religious beliefs, predominant mood (depressive, optimistic). Height, weight, and body mass index was also determined. Laboratory testing consisted of routine assays, general biochemistry-hematology and investigations such as EKG, EEG, abdominal ultrasound, echocardiography, CT as requested by the geriatrician. As first factor identified and responsible for longevity is genetic inheritance. We support the existence of longevity genes probably implicated in increases of resistance to noxious factors and regeneration capacity, but effects of these genes are likely dissimilar in magnitude and factors such as regulating genes and pleiotropic genes might play important roles in longevity. Also, very good vitamin D levels may be predisposing to longevity, especially as it influences transcription of some genes. Observations regarding coexistence of normal blood calcium range along with osteoporosis could have interesting implications in establishing vitamin D range. Dimorphic gender differences are sorting out in longevity and in this sense, sensitivity and robustness in counteracting noxious factors, are differing between genders. We subscribe to the concept regarding primary strategies in gerontology and geriatrics through prophylaxis interventions of which delay onset of diseases and disabilities. Thus, life span increase, due to late onsets of diseases, has the consequence of compressed morbidity as related to whole life course.
Key words: longevity, genetic inheritance, biochemical parameters, "optimal" aging

OBSERVAŢII PRIVIND UN GRUP DE PACIENŢI LONGEVIVI DIN INSTITUTUL NAŢIONAL DE GERONTOLOGIE ŞI GERIATRIE "ANA ASLAN"

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Rezumat. Scop: Identificarea prin investigaţiile unei echipe pluridisciplinare (medici geriatri, biologi, biochimişti, psihologi, sociologi) a unor factori care influenţează longevitatea umană şi care contribuie la îmbătrânirea "optimă", îmbătrânirea "de succes". Până în prezent, grupul de studiu a inclus 135 de subiecţi dintre care 115 cu vârste între 85 şi 89 ani şi 20 subiecţi în vârstă de 90-99 ani. Privind repartizarea pe sexe, au fost 111 femei şi 24 bărbaţi. Istoricul pacientului a constat în colecţia de date despre vârstă, luna naşterii, antecedente heredo-colaterale, dietă, status marital, fertilitate în cazul femeilor, vârsta primului ciclu şi a menopauzei, stil de viaţă, testare MMSE, credinţa religioasă, dispoziţia afectivă predominantă (optimistă, depresivă). Înălţimea, greutatea şi indicele de masă corporală au fost de asemenea determinate. Testarea de rutina de laborator a constat în clişeul general biochimie-hematologie şi investigaţii ca EKG, EEG, ecografie abdominală, ecocardiografie, CT la cererea geriatrului. Ca prim factor identificat şi responsabil pentru longevitate am evidenţiat moştenirea genetică. Susţinem existenţa genelor pentru longevitate probabil implicate în creşterea rezistenţei la factori nocivi şi capacităţii de regenerare, dar efectele acestor gene sunt inegale ca magnitudine şi factori precum genele reglatorii şi genele pleiotrope care pot juca roluri importante în longevitate. De asemenea niveluri foarte bune de vitamina D pot predispune la longevitate în special deoarece influenţează transcripţia unor gene. Observaţiile privind coexistenţa unui domeniu de normalităţi al calciului din sânge cu osteoporoza ar putea avea implicaţii interesante în stabilirea domeniului de valori pentru vitamina D. Diferenţele dimorfice de gen se conturează privind longevitatea şi în acest sens, sensibilitatea şi robusteţea în contracararea factorilor nocivi sunt diferite în cazul celor două sexe. Ne asociem conceptului privind strategiile primare din gerontologie şi geriatrie prin intervenţii profilactice care întârzie instalarea bolilor şi dizabilităţilor. Astfel creşterea duratei de viaţă prin instalarea târzie a bolilor are drept consecinţă compresia morbidităţii raportată la întreg parcursul vieţii.
Cuvinte cheie: longevitate, moştenire genetică, parametrii biochimici, îmbătrânire "optimă"

INTRODUCTION

Life span extension and life expectancy increases, once recorded in most of the worldwide countries, the need increased for studying aging in view of elaboration of strategies of social and medical interventions.

In Romania life expectancy is decreased by four to six years compared to the average life expectancy for Europe, namely 78.7 years for women and 71.6 for men in 2013, in comparison to 83.3 and 77.8 years respectively, for the European population according to the Center for Researches in Demography, of the Romanian Academy . The same study showed that between 1975 and 1990, life expectancy decreased in Romania. Even though after the World War II, life expectancy increased rapidly in former communist countries, this increase stagnated and even regressed in the period after the seventies, in which a social system impacted life expectancy at birth [1]. Romania was placed on the 109th position in a world ranking of life expectancies, while Monaco with a life expectancy of 89.7 years, and was placed first by this ranking.

For advanced countries it is estimated that in 2050, individuals over 65 years will be at least 25% of the population and in some regions even 40% and more.

At present the idea sorting out is that preventive medicine should be oriented towards those directions concentrated on morbidity, which anyway, cannot be reduced much during the stage preceding end of life. Before this aforementioned stage we may discuss on active, optimal longevity [2].

At the same time and as related to former old generations, positive attitudes of those who grow old, namely individuals born between 1946-1964, have been pointed out, these individuals being greatly interested in staying active, healthy, productive and independent as long as possible [3].

There are also less optimistic views. Thus, in a study conducted at Pew Research Center, 56% of US Americans interviewed asserted that they were no wishing to receive treatments for prolonging their lives. These answers were given due to perception that advanced ages come with disabilities, dependence, diseases and affliction [4].

Unfortunately, studies regarding aging and conducted in human subjects, especially those concerning longevity, are scarce because of difficulties to conduct them. It would be ideally to conduct longitudinal studies on a long term period.

At the National Institute of Geriatrics and Gerontology Ana Aslan, we have been conducting a study in longevous inpatients (aged over 85 years) admitted at the institute. Longevous individuals were selected, even though they may not form a representative population sample of the general population and an accurate evaluation of the longevous population is difficult to carry out. Despite these facts we managed to identify some factors that have influence on longevity and moreover, formation of a group of subjects who have been regularly admitted at the NIGG Ana Aslan and who, along with investigations, received treatment with the Romanian Gerovital H3 eutrophic drug (product). Regular longitudinal assessments of these longevous subjects could provide a picture on modes of actions of medical geriatric treatment and prevention at advanced ages.

MATERIALS AND METHODS

Aim of the study

To identify by way of investigations of a pluridisciplinary team (physicians geriatricians, biologists, biochemists, psychologists, sociologists) factors influencing human longevity and which contribute to a so-called "lucky, successful aging" or named according to some authors, "optimal" aging.

Together with clinical examinations, routine biochemical, hematological and immunological testing and cognitive assessments, investigations included a patient history consisting of data regarding food intakes, diets, lifestyle, education levels, religious beliefs, marital status, inherited diseases, blood group, month of birth and data about fertility in women.

Another objective of this research was establishing a bio-bank of human sera. In this view, blood samples collected were processed for obtaining sera according to specific techniques and frozen afterwards at -80 Celsius degrees. This biological material will be further used to identify markers of aging and longevity: molecular, biochemical and immunological.

Subjects

The study group until now included 135 subjects of which 115 aged between 85 and 89 years and 20 subjects aged 90 to 99 years. Regarding sex distribution there were 111 women and 24 men.

A patient history consisted of collection of data about age, month of birth, inherited diseases, diet, marital status, fertility in women, age at first period, menopause, lifestyle, MMSE testing, religious beliefs, predominant mood (depressive, optimistic). Height, weight and body mass index was also determined.

Laboratory testing consisted of routine assays and in addition investigations such as EKG, EEG, abdominal ultrasound, echocardiography, CT as requested by the geriatrician.

Patients gave their written informed consents for their data to be utilized in research statistics through complying with regulations concerning patient's safety and their rights.

RESULTS AND DISCUSSIONS

As first factor identified as responsible for longevity was heredity. Out of our subjects of this study, an overwhelming share of them had parents and siblings that lived more than 85 years, some of these latter mentioned being even centenarians. In this sense, our data were in accord with a series

of studies published in specialized literature [5].

Another series of studies conducted in invertebrates also supported the genetic inheritance of longevity and demonstrated that the aging process though complex, has a remarkable, surprising plasticity and can be accelerated, slowed, stopped or reversed under certain conditions [6, 7, 8]. Thus in mice, hundreds of aging modulating genes of longevity were identified [9]. A ten time extension of life span of nematodes was obtained [10]. In mice, life span increase by 50% by manipulating just one gene [9].

In humans, researches of last years concentrated on sirtuins, which are proteins playing important roles in regulations of metabolism of cells. Many scientists consider that sirtuin plays a key role in longevity extension that was noticed especially in caloric restriction experiments. There have been sustained efforts to identify alleles in longevous, centenarians, supercentenerians and in those managing with their degenerative diseases [11]. Such a study was conducted by a team of researchers from the Boston University, US. They studied DNA in 1055 persons aged more than 100 years and identified 150 genetic markers of longevity. After conducting the study researchers drew the conclusion that genes play increasingly important roles in establishing life span as much as individuals are beyond the age of 85. Authors of the above study let know that they will design a test by use of which, anyone could find out if there are genes encoding for long life in his genome.

Along with genetic factors, there are epigenetic factors which regulate genes' activities. Epigenetic factors are dependent on an individual's lifestyle but taking into account that epigenetic factors are genetically transmitted, lifestyles of former generations, besides genes, could have influence on longevity.

As concerns pathologies encountered in persons aged over 85 years, bone and joint diseases coxarthrosis, gonarthrosis, the onsets of which were after ages of 50 and 60 years, were placed first according to their frequencies. As regards biochemical and hematological parameters, most of these octogenarian patients clearly and statistically significantly as compared to the general population, had glycemia and total cholesterol, HDL-Cholesterol and LDL-Cholesterol within normal ranges or at upper or slightly beyond limits (Tab. I).

Tab.I Average values of several routine clinical biochemistry parameters in the study-group longevous patients (n=135)

Glycemia (mg/dl)	Total Cholesterol (mg/dl)	LDL-Cholesterol (mg/dl)	HDL-Cholesterol (mg/dl)	Triglycerides (mg/dl)	AST (IU)	ALT (IU)	Creatinine (mg/dl)	Uric acid (mg/dl)
102 + 20	190+24	112+14	55+10	104+19	22+10	14+6	1.01+0.17	5.40+1.55

As well, majority of subjects presented with osteoporosis confirmed by DEXA or radiological examinations. In this sense, patterns of degradations of tissues and organs in aging are figuring out. Inflammations of joints followed by differentiation and regeneration as affected by inflammation at these localizations are phenomena of extremely high risk for aging. Likewise, osteoporosis which is primarily demineralization of bones is such a phenomenon of degradation through disinhibiting osteoclasts as a consequence of deficits in sexual hormones that function as growth factors. Even though affecting the locomotor system impedes locomotion

and affects also the quality of life it does not threaten survival. Same with mechanical devices, the wear out of components that are in locomotion occurs before the wear out of the engine. But wear out of the engine impedes life of the vehicle. Likewise for organisms, functioning of the cardiovascular system as well as relative access to nutrients meaning glucose, assures survival.

Therefore, as our results and those of studies of the specialized literature showed, a relatively healthy cardiovascular system and a relative sensitivity to insulin as reflected by normal glycemia are determinants of survival. In absence of statins treatments, reduction in importance of conventional cardiovascular risk factors evaluated as values of cholesterol (total, HDL-C, LDL-C), triglycerides is nevertheless almost omnipresent. There were no data on homocysteine which is another cardiovascular but not only, risk factor. On the other hand, also regarding the cardiovascular risk, the majority of longevous patients was statistically significant normal weight. We had few incomplete data regarding the ratio waist/hip. But we can infer a higher sensitivity to insulin of these patients than that of the general population, especially in men who without exception were normal weight. Also in the case of men demandings as related to aging were different. According to our processed data, no man patient had diabetes and/or hypercholesterolemia or was overweight although in women patients there were few such cases. Elderly women present with protective mechanisms which allow for having cardiovascular risk factors without affecting their health conditions. Women have higher levels of some antioxidant enzymes (SOD forms) and protection as provided by estrogens before menopause has its long term effects. Interestingly, there were some smokers among these patients but smoking was almost absent among women patients. There are gender differences as regards noxious effects of some substances. Women are more vulnerable to smoking's noxious effects, as some studies showed. However, there are exceptions to the aforementioned, the most persuasive being that of Jeanne Calment who was 122 years when she died, and those of longevous women who smoked.

Data regarding comorbidities and pathologies in these longevous will be topics of a distinct paper attempting to establish possible correlations.

Another interesting aspect concerning results of this study was normal total and ionized calcium levels in these longevous patients. Even though vitamin D was not but is going to be assessed, we can infer that deficit of vitamin D, which is very frequent in the European population, should be considered in a different manner in these subjects. Recent data suggested that vitamin D effect would be similar to that of IGF1 and so, this vitamin would function as a growth factor being related to insulin pathways and hence mimicking sensitivity to insulin [12].

On the other hand, other recent data suggested that vitamin D would activate many genes the expression of which is affected in aging [13].Actually, vitamin D would influence cellular response to stress as reflected by proteins solubility which is implicated in degenerative diseases such as Alzheimer's disease. Vitamin D, 25-hydroxyvitamin D deficit increases risks for diseases related to aging such as Alzheimer's, Parkinson's, cognitive impairment and cancer. These data make sense if we take into consideration the biochemical hypothesis of aging we recently asserted [14]. Hence, some cellular reactions' diminishing, which arises from functioning of the organism

depending on ecology of a species and that subsequently affects cell's energy state and further other reactions would determine aging. Interpretation of the vitamin D action in the context of aging likely means this vitamin would be implicated in both restoring cellular reactions (genes' activation) and energy delivery through its action similar to IGF1. Likewise, data on low sensitivity to insulin which is frequently encountered in longevous would be in accord with the above mentioned hypothesis. Sensitivity to insulin actually translates to cell's energy and cells' access to glucose. Sensitivity to insulin decreases with age and this fact is as well in accord with the above hypothesis. Lack of vitamin D has been associated with degenerative diseases (multiple sclerosis) but also with schizophrenia [15] which has been related as well with impaired insulin/ IGF1signalling pathway. A great share of investigated longevous were coming from rural areas, so working in agriculture, gardening and therefore being exposed to sunlight had consequences on synthesis of vitamin D. On the other hand, the majority of these longevous subjects admitted that although they didn't eliminate meat from meals they had a diet which would be considered preponderantly lacto-vegetarian. Other studies also were in support of lacto-vegetarian diets being protective against age-related pathologies, so in favor of longevity. Nevertheless, studies (the China study) challenged the above assertion and expressed reservation concerning consumption of dairies, which has been associated to acidosis and osteoporosis. But China study as it was named was conducted in several Chinese regions, in Asian population the diaries' consumption of which, is poor. The majority of Asian people, in their adulthood, suffer from intolerance to lactose. Dairies' consumption is reduced traditionally in these populations, while in Europe it is thousands years old. And this fact is not just about intolerance to lactose, which is reduced as presence in Europeans. As transition to agriculture in populations of hunters-harvesters would have had influence on genetics and epigenetic on long-term, the same could have happened in the case of populations' diaries' consumptions [16]. Traditional diets of Europeans include many diaries and occasionally meat. Longevous of this study- group admitted that all life-long they had diets very alike to traditional diets of this area (European southeastern and especially rural areas).

We did not have sufficient data about religious beliefs, affiliation and especially adherence to fasting as imposed by religion. Some women patients told they were fasting at least one a week, on Fridays. Fasting, especially that with long intervals between two meals could promote autophagy, which is important effect of caloric restriction [17]. Autophagy, having effects of repair, is also according with the biochemical hypothesis on aging as autophagy promotes reactions which occur under critical conditions.

After numerous studies conducted on a large number of laboratory animals, researchers discovered the most efficient method for life span extension: caloric restriction. A very low calories diet but which contains an adequate amount of proteins, vitamins and minerals leads to a longer life span [18]. This aforementioned effect was first observed in 1935 in laboratory experiments conducted in mice. Those mice subjected to a strict diet, which received minimum amount of calories lived by 40% longer than mice with unrestricted access to food. Since then the method was tested in numerous other

laboratory mammals, the obtained effect being the same regardless the species.

In a study conducted in monkeys, those which lived for 20 years after being subjected to low calories diets were healthier, with fewer cases of laboratory animals having diabetes and cardiac diseases than monkeys which had normal calories amount diets. In assessments conducted in humans, researchers discovered that reducing calories consumed has as well other positive effects besides delaying the aging process; reducing calories has anti-inflammatory effect, reduces the risk of atherosclerosis and leads to improvement of memory. Jiroemon Kimura, a Japanese aged 114 years having the distinction of "the oldest old man alive" asserted that the secret of longevity is small serving meals.

In our study regrettably, we did not have sufficient data on patients' blood groups which would be implicated in inflammatory and pro-coagulant processes. There are several studies in different populations (Europeans and Asian) that showed an association of blood group B with a greater life expectancy. What is interesting about this blood group, which is found out in larger shares of longevous than that for the general population [19], is that it does not seem to be associated with survival as usually [20]. The aforementioned means that among patients admitted to a hospital, those with blood group B due to several reasons had smaller chances to survive. This latter mentioned among other findings call into question the Finch and Austad criteria for detecting aging, according to which a species is aging if fertility decrease with age and increase in mortality are evident. But, especially in species that are aging, phenomena leading to degeneration associated with aging, as mechanisms of instant survival of species, can for short term save the individual from dying. Capacity to maintain high glycemia and cholesterol under critical conditions has effects of saving life on short term and same is valid for coagulation and even inflammation. The above mentioned does not mean that the Austad and Finch criteria have no validity but a new clearer theory on aging is needed based on what takes place at biochemical levels. As related to the criterion of fertility there is also a phenomenon which extends life span and by delaying aging reduces fertility. This phenomenon is caloric restriction and laboratory animals subjected to caloric restriction lived longer but their fertility decreased. This phenomenon is likely to take place in the course of evolution. Generally, a longer life span in a species positively correlates with a decreased fertility. Another aspect which deserved being noted was that related to month of birth. As risk to develop certain disorders depends on month of birth (in relationship with seasonal variations of some hormones, such as IGF1), as well longevity seems to be related to month of birth. According to data of specialized literature, a greater number of study-group longevous, than those of general population, were born in October and November. For interpreting this phenomenon we referred to results of a longitudinal study also on longevity, which was conducted in the US over several generations. A conclusion of the above North-American study was that balanced and conscientious individuals are found out more often among longevous. People born in the fall would be more collected and conscientious than the others. So they would have a better control over their behavior, thus promoting survival any time but also favoring a better management of stress. Certainly, there could be biochemical aspects and the above behavioral and psychological aspects were

issued from personal observations, on which to go over through future studies. We already pointed out dimorphic gender differences in aging, the very first being life expectancy. There are studies which attempt to provide explanations on aforementioned topic, of which one of the most complex is the study conducted by Maklakov A et al. [21].

According to results of our study, generally longevous men were normal weight and even though they presented with age-related pathologies of the cardiovascular system, bone and joints, digestive systems, with no exceptions they had ideal, blood glucose and lipids normal values. Also, the ratio waist/hip within normal ranges, in cases for which it was measured, favored sensitivity to insulin. There was a tougher selection of longevous men than that of women longevous in that at least some risk factors affected much longevous men. Most of longevous men were non smokers but some of them admitted they smoked in the past. Usually, cardiac disease was more complex in longevous men but degenerative factors like hyperglycemia and dyslipidemia were rare in these. It is interesting that in longevous men, increased incidence of gastric ulcers was highlighted not only in past patient history and if proven as statistically significant, could be relevant regarding longevity in men. Among longevous men a good mental state was noticed along with good MMSE scores. An increased share of longevous men had higher education but also those who did not have were noticed for their mental robustness in the past and present as proven by their attitudes and personal histories. According to data of specialized literature, longevous men were most often married and marriage seems to be beneficial for longevity in men.

CONCLUSIONS

From results obtained by now we can draw several conclusions:

First factor identified and responsible for longevity is genetic inheritance. An overwhelming share of our subjects had parents and siblings who lived more than 85 years, some of them even being centenarians. We support that there may be longevity genes probably implicated in increases of resistance to noxious factors and regeneration capacity but effects of these genes are likely dissimilar in magnitude and factors such as regulating genes, pleiotropic genes might play important roles in longevity. Longevity genes should be investigated with regard to cell necrosis, cell survival and so, resistance to apoptosis, at least in the case of some tissues and systems such as the nervous system.

We showed positive correlation of longevity with normalcy of cholesterol and glycemia. Also, benefits of lacto-vegetarian diets were pointed out. The observation regarding coexistence of normal blood calcium range along with osteoporosis could have interesting implications in establishing vitamin D range but not presently confirmed because of lacking data on vitamin D levels in these longevous. Could it be a hormonal mechanism which releases calcium from bone and thus protects the organism against harmful deficits of calcium? Could it be a matter of diets?

On the other hand, new data showed that vitamin D increased vigor in the cold season being also a protective effect against infections. Hence, vitamin D may be predisposing to longevity especially as it influences transcription of some genes (vitamin D would function as a growth factor-IGF1 taking into account insulin signaling pathway, therefore would be mimicking sensitivity to insulin).

Also, influence of month of birth on longevity was confirmed. Our data indicated October and November as most frequently encountered months of birth in longevous.

As well, dimorphic gender differences are sorting out in longevity with sensitivities and in this sense, robustness in counteracting noxious factors, are differing between genders. Regarding longevity a clearly dimorphic gender difference was evident, namely preponderance of women in the study-group.

Gender differences are very important and concerning cells, tissues the whole organism and the DNA expression is considerably different depending on sex.

We subscribe to the concept some authors designed regarding primary strategy in gerontology and geriatrics in order to extend life span, namely through interventions of prophylaxis which delay onset of chronic diseases and disabilities. Thus, life span increase due to late onsets of diseases has the consequence of compressed morbidity as related to whole life course.

To achieve optimal longevity (live longer but in good health), healthy life span should significantly increase.

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THE LIFE STYLE AND HEALTH STATUS CONNECTED TO ELEMENTS OF THE LIPID PROFILE

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Abstract. In social sciences, the "lifestyle" concept defines the human being as a whole. It may represent also an optimal approach for gerontology studies. Our work points out the links between the lifestyle, chronic pathology and the lipid profile. A number of 199 NIGG patients, mostly women (X=69.21 years) are assessed by medico-social tests for physical, psycho-social functionality and nutritional status. Clinical diagnoses and laboratory analyses are collected from the clinical records. We highlight some significant correlation: cholesterol values decrease with age (r=-.214/ p=.002); MNA-score and SLIQ-score (Simple Lifestyle Indicator Questionnaire) directly correlate with total-cholesterol and HDL, proving their decline in malnutrition and poor lifestyle. Regarding physical functioning, we find significant links between total-cholesterol and LDL with Handgrip strength, Up and GoTest and Physic Activity Score (SLIQ). We find negative correlations between lipids and psycho-emotional functioning, ilustrated by MNA items, such as: nutritional state self-assessment (MNA-o), psychologic stresses (MNA-d: r=.218/p=.002) and neuro-psychologic problemes (MNA-e). We also find an inverse link between total cholesterol and hours of night sleep (r= -.144/ p=.042) that shows the negative effect of fatigue on the increase in cholesterol level. Significant links between alimentary habits and lipids are given by: LDL – fats consumption (r=.171/p=.016), HDL – alcohol consumption (r=.170/p=.016) and HDL – fruits/vegetables consumption. We must underline the negative relation between cholesterol and cognitive disorders; literature data show marked decrease of the cholesterol as a risk factor for dementia. The work reveals the importance of lifestyle in the appearance of dyslipidemias, besides genetic determination. Therefore, their prevention involves a physically and psycho -social active life, a healthy diet, and when necessary, drug therapy too.

Key words: lifestyle, global health, lipid profile

STILUL DE VIAŢĂ ŞI STAREA DE SĂNĂTATE OGLINDITE PRIN ELEMENTE ALE PROFILULUI LIPIDIC

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Rezumat. În definiţia conceptului "stil de viaţă" din ştiinţele sociale, omul este privit ca un întreg. Abordarea este optimă şi în studiile de gerontologie. Lucrarea prezintă unele legaturi dintre stilul de viaţă, sănătate şi profilul lipidic al pacienţilor. 199 pacienţi din INGG, în majoritate femei (X=69,21 ani) au fost evaluaţi prin teste medico-sociale privind funcţionalitatea fizică, psiho-socială şi statusul nutriţional. Diagnosticele şi investigaţiile biologice sunt culese din clinică. Se observă unele corelaţii semnificative: valorile colesterolului descresc cu vârsta (r= -.214/ p=.002); scorul MNA şi scorul SLIQ (Chestionar Simplu al Stilului de Viaţă) corelează direct cu colesterolul total şi HDL, sugerând scăderea lor în malnutriţie şi stil de viaţă scăzut. În privinţa funcţionalităţii fizice, găsim legături semnificative între colesterolul total şi LDL cu evaluările: Forţei de compresiune palmară, Vitezei de mers şi de transfer şi Scorului de activitate fizică (SLIQ). Se observă corelaţii negative între lipide şi funcţionalitatea psiho-emotională, ilustrate de itemi MNA: autoevaluarea stării nutriţionale (MNA-o), stres

psihologic (MNA-d; r=.218/ p=.002) şi probleme neuro-psihologice (MNA-e). De asemenea, am găsit o corelaţie inversă între valoarea colesterolul total cu numărul orelor de somn (r= -.144/p=.042), subliniind efectul negativ al oboselii, care creşte valorea colesterolului. Legături semnificative între lipide şi obiceiurile alimentare sunt date de: consumul de grăsimi şi valoarea LDL (r=.171/p=.016), cantitatea de alcool şi HDL (r=.170/p=.016) şi consumul de fructe/vegetale şi HDL. De evidenţiat legătura inversă între colesterol şi tulburările cognitive; datele din literatură susţin că valorile scăzute ale colesterolului reprezintă un risc crescut pentru demenţă. Lucrarea relevă importanţa stilului de viaţă în apariţia dislipidemiilor, pe lângă determinarea genetică. Prin urmare, prevenirea lor presupune o viaţă activă din punct de vedere fizic şi psiho-social, o alimentaţie sănătoasă, iar când este cazul, şi terapie medicamentoasă.
Cuvinte cheie: stil de viaţă, sănătatea globală, profil lipidic

INTRODUCTION

Worldwide, the dramatic change in the environment and human behavior has brought a true epidemic of obesity and type 2 diabetes (diabezity) [1]. Both diseases are cardiovascular risk factors, and contribute to the cardiovascular (CVD) epidemic, "the most important epidemic known by humanity, of enormous proportions, increasingly affecting young subjects" (WHO 1969).

In 2006, the European Parliament launched the "European Heart Health Charter" defining the profile of an individual for maintaining health as: non-smoking; adequate physical activity-at least 30 minutes, five times a week; healthy eating habits; without excess weight; blood pressure below 140/90 mm Hg; serum cholesterol below 190 mg / dl; normal glucose metabolism; avoiding excessive stress [2].

In medical practice, cholesterol and triglycerides are usually measured, as their elevated values are risk factors for CVD. Therefore, generally, cholesterol is perceived as a great health enemy. But in fact, it has valuable functions in organism: essential constituent of the cell membrane, precursor of bile acids, steroid hormones and Vitamin D3.

● Cholesterol may be of food origin, but in larger quantities it is synthesized in the body, especially in the liver.

● There are secondary dyslipidemias with low cholesterol:

- Lack of synthesis - in hepatic impairment;
- High consumption in case of cellular regeneration - severe anemia, cancers, pregnancy;
- Excessive burns - hyperthyroidism;
- Intestinal disorders - absorption or loss;
- Malnutrition.

● Diseases in which cholesterol is increased: obesity, diabetes mellitus, hypothyroidism, nephrotic syndrome, and the consequence of using some medicines (diuretics, some β-blockers, corticosteroids, oral contraceptives) [3].

● Lifestyle can also generate hyperlipidemias:

- Excessive alcohol consumption (which causes inhibition of oxidation of free fatty acids and increases in triglyceride levels);
- High fat saturated diets;
- Stress, anxiety;
- Smoking.

In the last decades, much has been said about the metabolic syndrome, which is a set of risk factors: abdominal obesity, reduced glucose metabolism (increased blood sugar and/or insulin resistance), dyslipidemia and hypertension. Patients with this syndrome have an increased risk for type 2 diabetes, cardiovascular disease and premature death [4].

Serum cholesterol relationships with cardiovascular disease and dementia

Through the 1950s -1960s, physiologists have differentiated two types of cholesterol-binding lipoproteins: low density lipoprotein (LDL) and high density

lipoprotein (HDL). Epidemiologists have shown that high LDL values predispose to myocardial infarction, and high amounts of HDL are protective.

Michael S. Brown and Joseph L. Goldstein received the Nobel Prize in 1985 for a breakthrough on regulating cholesterol metabolism, via an LDL receptor on the cell surface.

They began by showing that homozygous patients with Familial Hypercolesterolemia (very rare disease, occurring in 1:1 million cases) have plasma levels of cholesterol 6-10 times over normal. They make early myocardial infarctions. Their early atherosclerosis does not have another risk factor (e.g. as: smoking, HTA, diabetes mellitus, type A personality). It is the genetic official proof of its determination only through LDL [5].

Many researchers have suggested that serum lipids play a key role in the immune system. On the other hand, the presence of cholesterol is more and more common as an inflammatory response of intimate arterial injury, and represents a decisive step in the genesis of arteriosclerosis. The infections can represent such injuries.

These two concepts are difficult to harmonize with the hypothesis of the LDL receptor by which LDL is the decisive factor of arteriosclerosis. However, some observations on the conflict with the LDL receptor hypothesis can be explained by the idea that LDL and/or high total cholesterol (TC) are protective against infection.

According to the atherosclerosis hypothesis by modified response to injuries, there are at least two pathways that explain inflammatory and proliferative lesions of intimate artery. The first involves the interaction of monocytes with platelets, induced by hypercholesterolemia. The second involves direct stimulation of endothelium by several factors: smoking, diabetes mellitus, hyperhomocysteinemia, excess iron, copper deficiency, oxidized cholesterol, microorganisms. The action of everyone is supported by evidence, but the degree of participation is unknown. However, there is sometimes a lack of exposure response in observational studies linking LDL changes to clinical and angiographic responses; or the negative link between cholesterol changes and angiographic changes. Otherwise, there is a significant increase in atherosclerotic lesions following dietary cholesterol lowering, and above all, more increasing longevity than elderly mortality is predicted by high cholesterol. The most likely explanation is the beneficial influence of cholesterol on the immune system [6].

Relations between cholesterol, dementia and other health problems are controversial at present. Also, the benefit/risk ratio for cholesterol-lowering medicines in the elderly is still questionable. A longitudinal study initiated in 1972 (Cardiovascular Risk Factors, Aging and Dementia Study) had the last re-evaluation after 21 years [7]. It showed that high total cholesterol values in middle age are a risk factor for subsequent dementia and cognitive impairment. The meaning of cholesterol differs in young people comparative to the elderly, especially for those with normal or low cholesterol and not for those with high cholesterol. The low-cholesterol group is a mixture of people with low levels of cholesterol in all their life, along with people with low cholesterol secondary to diseases (including Alzheimer's). Those with high total cholesterol have a risk of vascular disease at advanced age, benefiting from statin therapy in old age. Interpretation of low total cholesterol at advanced ages should be done taking into account both their health and their cognitive status. Therefore, therapeutic

guidelines for both dementia and CVD are required.

The results of the Whitehall II Study (started in 1985) show low levels of HDL (<40 mg/dL) which are associated with poor memory in middle-aged adults [8]. Furthermore, decline in HDL was associated with declines in memory over a 5-year period. The National Cholesterol Education has stressed the importance of lowering LDL to reduce the burden of cardiovascular disease. The researchers suggest that increasing HDL might also be important, for cognitive outcomes in particular.

Objectives: The study of links between lifestyle and global health, as well as their relationships with the patient's lipid profile.

MATERIALS AND METHODS

The lot of 199 NIGG patients consists of 27 males and 172 women, aged between 45 and 92 years (X = 69.21 years). Diagnostics and biological investigations are collected from the clinic.

The lot is evaluated globally, using a medico-social approach through tests focusing on:

• The lifestyle: - The Simple Lifestyle Indicator Questionnaire (SLIQ) [9];

• The Nutritional Status - Mini Nutritional Assessment (MNA) and Waist-hip index [10];

• Physical functionality:

- ADL (Barthel), IADL (Lawton & Brody);

- Timed Up and Go Test;

RESULTS AND DISCUSSIONS

1) The prevalence of chronic conditions

The prevalence of chronic conditions is analyzed by age groups, ordering the prevalence after the values for the older group (70-95 years). In these subjects, cardiovascular diseases have the highest prevalence and the difference between the two age groups for CVD was particularly high: 124%. Percentage differences are also noted in neurological diseases: there were 50% more subjects with neurological diseases within the older age group, compared to "the younger elderly". The fact can be explained by the atherosclerotic pathology that increases with the age. The large differences between age groups for cardiovascular and neurological pathology suggest that, in their youth, subjects tend to have certain unhealthy behaviors that later generate cardiac and neurological circulatory diseases. In endocrine-metabolic pathology, the younger group surpasses the older one by 57.5%.

2) The nutritional status

a) Evaluation by waist-hip ratio

The waist-hip ratio assesses besides nutritional status the cardiovascular risk; with aging, a progressive increase of this risk can be noted (Tab. I).

Tab. I Significance of waist-hip index evaluation (abdominal obesity) by age group

Waist-hip index	45-59 years	60-69 years	70-92 years	Total
Low cardiovascular risk	29.0%	15.4%	9.5%	14.1%
Moderate cardiovascular risk	32.3%	38.5%	39.7%	38.2%
High cardiovascular risk	38.7%	46.2%	50.9%	47.7%
Total	100.0%	100.0%	100.0%	100.0%

An important difference of percents, almost three times higher appears for high CVD risk, in women (64.0%), compared to the same risk level in males (22.0%) (Tab. II).

Tab. II Significance of waist-hip index evaluation by genders

Waist-hip index	**Men** {%}	**Women** {%}
Low cardiovascular risk	51.9	9.9
Moderate cardiovascular risk	25.9	26.2
High cardiovascular risk	22.2	64.0
Total	100	100

b) Evaluation by Body Mass Index (BMI)

We found that there are subjects with normal weight- only one fifth of the sample. Higher weight subjects represent 78.6% of the sample: obesity with its three levels of assessment summed up (41.1%) + overweight (37.5%). The proportion of women with abdominal obesity (89.3%) correlated significantly with high overweight in women (78.4%) (r =.168 / p =.018) (Fig.1).

Obesity is evenly distributed across all age groups of the sample. In the "over 70 years" group, with a high prevalence of cardiovascular and neurological diseases, we suppose that more cardiovascular risk factors exist. But since those under the age of 70 have high proportions of obesity, an increase in CVD prevalence is expected for them as well, with advancing age. Moreover, the diabetes is more prevalent in their group. Specifically, a double weight appears: 37.5% in "45-69 years" group compared to 19% in the "over 70 years" group.

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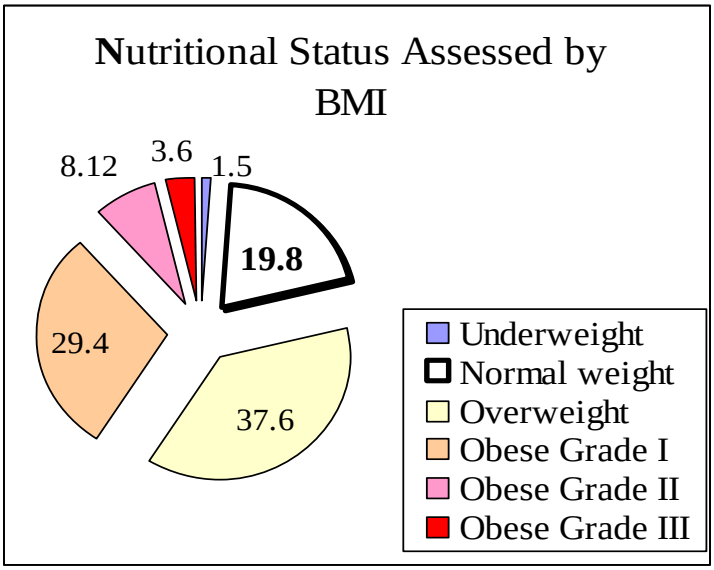

Fig.1 Nutritional status assessed by BMI

3) The metabolic syndrome

The metabolic syndrome (MS) was evaluated on the basis of the National Cholesterol Education Program's Adult Treatment Panel III report (ATP III). ATP III criteria bring a simplified definition for clinical use. People who meet three of the below criteria are included in the diagnosis MS:

- High blood pressure (>130/85 mm Hg),
- Low serum HDL (<40 mg/dL in men, <50 mg/dL in women),
- High serum triglyceride levels (≥150 mg / dL),
- Very high plasma glucose (> 110 mg / dL) and
- Abdominal obesity (waist circumference >102 cm for men and >88 cm for women).

In Tab. III we note the increasing in the frequency of the syndrome with age (women are the majority in the lot).

Tab. III The metabolic syndrome- distribution by gender and age groups

Group	Metabolic syndrome	45-59 years	60-69 years	70-92 years	Total
Men	absent	-	25.0%	75.0%	100.0%
	present	27.3%	45.5%	27.3%	100.0%
Women	absent	20.9%	33.7%	45.3%	100.0%
	present	**8.1%**	**44.2%**	**47.7%**	100.0%

4) Lifestyle and European Heart Health Charter

From the study data regarding lifestyle assessment we obtained the results from Tab. II. We can see that overweight, high cholesterol, high blood pressure, unhealthy nutritional habits and the sedentariness are the biggest enemies of a healthy lifestyle?

Tab. IV The extent to which our patients fulfill the Charter's recommendations

The recommendations of Heart Health Charter	%
No smoking	87.9
Avoiding excessive stress	80.4
Normal glucose metabolism	71.4
Adequate physical activity	35.5
Healthy Eating Habits	34.7
Blood pressure<140/90 mmHg	34.2
Total cholesterol<190mg/dl	33.2
Without overweight	21.4

5) Correlation analyses of lipid profile and data on health and lifestyle

In the literature, there are transversal and prospective studies showing that TC and LDL begin to decrease in men over 60-65 years and in women over 70-75 years. Some authors have suggested that frailty or chronic diseases lie behind the declining cholesterol levels in old age. But, in The Turku Elderly Study [11], a Finnish longitudinal study conducted between 1991 -2006, all the 221 subjects, from the

last evaluation, 85 ages old were still home-residing and had good general health status. (And they did not use statins). Thus, it seems unlikely that the decline in TC and LDL was caused by disease or frailty, particularly when HDL simultaneously increased.

In our study, TC decreases with age (r = -214 / p = .002). Component fractions, also decrease, each correlating weaklier with age. So, for LDL: r = -.151 / p = .034 and for HDL: r = -.155 / p = .029. Between all serum lipids, only HDL correlates significantly with the frailty score (GFI score) (r= -.163 /p=.029). The relation shows the trend of "good" cholesterol to decrease in frailty (Tab. V, Tab. VI).

Tab. V Correlations between total cholesterol and LDL-cholesterol with chronic pathology and lifestyle elements

Total-cholesterol correlated with	**r=**	**p=**		**LDL cholesterol correlated with**	r=	p=
Age	-.214	.002		**Age**	-.151	.034
Chronic pathology				**Chronic pathology**		
Cardiovascular diseases number	-.237	.001		Cardiovascular diseases number	-.208	.003
Heart failure	-.205	.004		Chronic venous insufficiency	-.165	.020
Endocrino-metabolic diseases	.177	.012		Heart failure	-.157	.027
Ischemic heart disease	-.176	.013		Sequelae of stroke, cerebral arteriosclerosis	-.153	.031
Chronic venous insufficiency	-.165	.020		Ischemic heart disease	-.136	.050
Cognitive impairment	-.165	.020				
Sequelae of stroke, cerebral arteriosclerosis	-.159	.025				
Waist-hip Ratio (abdominal obesity)	.162	.023				
Lifestyle elements:				**Lifestyle elements:**		
MNA_H (nr. medicines>3)	.214	.002		MNA_H (nr. medicines>3)	.203	.004
Palmar compression force	.190	.014		Palmar compression force	.177	.023
Walking and transfer speed test	-.170	.019		Fatty foods consumption	-.171	.016
MNA_E= neuropsychological problems	.156	.028		Walking and transfer speed test	-.163	.024
Fatty foods consumption	.153	.032				
MNA_L (2 servings and over vegetals/day)	-.146	.039				
Nutritional score (MNA)	.145	.040				
Night sleep hours	-.144	.042				

Regarding the link with the chronic pathology, there is a significant relationship with the cardiovascular diseases: ischemic heart disease, chronic venous insufficiency, sequel of stroke, cerebral and systemic arteriosclerosis and heart failure. But with these conditions inversely correlate, contrary to LDL receptor theory, whereby LDL is considered the determining factor of atherosclerosis and the diseases it generates. A possible explanation would be the decrease in serum lipids by statin therapy, widely used for the cardiovascular and dismetabolic pathology of our subjects (Tab. V, Tab. VI).

Abdominal and general obesity (assessed by waist-hip ratio and BMI) correlates only with HDL values and with triglyceride levels (Tab. VI).

Negative correlation of TC with cognitive impairment (r = .165 / p = .020) (Tab. III) matches the data in the literature already mentioned in the introduction. (A Finnish study/2006 that shows: ”decreasing serum TC after midlife may reflect ongoing

dementia processes and may represent a risk marker for late-life cognitive impairment“) [7].

Regarding the links with elements of lifestyle that led, over time, to the chronic pathology, we recall:

-SLIQ is significantly linked to HDL (r=.172 /p = 0.015), suggesting the importance of all lifestyle components in lipid metabolism (Tab. VI).

-MNA nutritional score directly correlates with TC and HDL, suggesting the decrease of these lipids in malnutrition (Tab. VI).

-Significant links also exist between eating habits and dyslipidemia. The study reveals relationships with harmful effect between: excessive fat consumption and LDL (r=.171/p=.016), between the amount of alcohol and HDL (r = -171 / p = .016) and a beneficial link between fruit / or vegetable and HDL consumption (Tab. V, Tab. VI).

Tab. VI Correlations between HDL and triglycerides with chronic pathology and lifestyle elements

HDL–cholesterol correlated with:	r=	p=		**Triglycerides correlated with:**	r=	p=
Age	-.155	.029				
Chronic pathology				**Chronic pathology**		
Abdominal obesity	-.225	.001		Metabolic endocrine diseases	.324	.000
Osteoporosis	.208	.003		Peripheral arterial disease	.219	.002
Heart failure	-.194	.006		Obesity (BMI)	.211	.006
Number of heart diseases	-.191	.007		Diabetes	.201	.004
GFI_Score (frailty)	-.163	.022		Abdominal obesity	.190	.007
Hypertension	-.143	.044		Number of diseases	.165	.020
				Hypertension	.165	.020
Lifestyle elements:				**Lifestyle elements:**		
MNA-d (psychological stress)	.218	.002		MNA-o: Self assessment of nutritional status	-.162	.023
Exercise Score	.216	.002				
Self assessment of physical state (GFI)	.207	.003				
Nutritional score (MNA)	.200	.005				
Lifestyle Index (SLIQ)	.172	.015				
Vegetable consumption index (from SLIQ)	.137	.050				

-In terms of physical activity, we find significant relationships between TC, LDL and HDL with assessment of: physical activity score (SLIQ) (r = .216 / p = .002), palmar compression force (r=.190/p=.014), walking and transfer speed (from Timed Up and Go Test) (r = .170 / p.019) (Tab. V, Tab. VI).

-The psycho-emotional functionality illustrated by item MNA-d (psychological stress from the last 3 months) significantly correlates with HDL (r = -.218 / p = .002) and with triglycerides (r = .139 / p = .050) (Tab. VI). Insufficient sleep is strongly linked to the presence of stress. TC correlates negatively with the number of sleep hours (r= -.144/ p=.042) revealing the negative effect of fatigue, which can lead to hypercholesterolemia (Tab. V).

-The use of some medicines (diuretics, some β-blockers, corticosteroids) may increase cholesterol. In our lot, the item MNA-h, representing the daily consumption of over 3 types of drugs, significantly correlates with TC and LDL (r=.214 / p=.002). Most likely, hypercholesterolemic medications are included in lot therapy (Tab. V).

CONCLUSIONS

● High prevalence of overweight and obesity (37.6% respectively 41.2%). Assessing abdominal obesity suggests increasing cardiovascular risks as the subjects' age progresses.

● The metabolic syndrome is present in over half of the subjects, highlighting the risk of diabetes, along with CVD.

● In the 45-69 age group, the endocrine-metabolic pathology has a higher prevalence, whereas in the elderly, between 70-92 years, the high shares of cardiovascular and neurological pathology are observed.

● The inverse proportional link between cholesterol and CVD is contrary to the theory that considers LDL as determining factor of atherosclerosis, but for hospitalized patients, cholesterol lowering can be explained through hypocholesterolemic therapies.

● The negative link between TC and LDL highlight that lowering cholesterol in the elderly would be a marker of the risk of cognitive impairment.

● Correlation analyses have demonstrated the existence of links between the lifestyle (physical activity, eating, alcohol consumption, smoking and stress) and the lipid profile of the subjects.

We can synthesize that besides genetic causes, dyslipidemias can also have life-related causes, such as inappropriate lifestyle elements. Therefore, dyslipidemias can be prevented by correcting those unhealthy life habits. It goes without saying that, besides the hygienic-dietary approach, the drug therapy is supplemented where necessary.

Acknowledgment

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ATHEROSCLEROSIS PROGRESSION INDICATORS IN SENESCENT PATIENTS

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Abstract. Inflammatory process and lipid peroxidation are collaborative events involved in atherosclerosis (ATS) development. Atherogenic indices: Castelli risk index I-CRI, Castelli risk index II-CRII, Atherogenic index-AI and Atherogenic coefficient-AC are good predictors of future cardiovascular events. The aim of the study was to assess lipid profile and atherogenic indices, in senescent patients with carotid ATS, in correlation with HeartScore and total atheromas area. We were taken into the study: group with carotid atherosclerosis-ATS1; group with carotid atherosclerosis and advanced stenosis-ATS2 vs. control group-C without significant atheromas. We obtained increased values of cholesterol and LDL-cholesterol at ATS1 vs. C and a decrease HDL-cholesterol levels at ATS2 vs. C. Moreover, AI and HeartScore are elevated in ATS2 vs. C. For all groups, AI has a value above 0.24 which is associated to a high risk for all patients included in the study. HeartScore indicated an intermediate risk for ATS1 and a high risk for ATS2. Linear regression equation revealed a positive significant correlation between HeartScore and AC, AI, CRI at ATS1. As for ATS2 there is a positive significant correlation between atheromas area and AC, CRI, CRII. AI can contribute as a cardiovascular risk marker to predictive/prognostic value better than individual lipids. All this data highlighted that atherogenic indices are strong indicators of cardiovascular disease risk and there is a direct correlation between HeartScore and ATS progression.
Key words: atherogenic indices, HeartScore, atherosclerosis

INDICATORI AI PROGRESIEI ATEROSCLEROZEI LA PACIENŢII SENESCENŢI

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Rezumat. Procesul inflamator şi peroxidarea lipidelor sunt evenimente cooperante implicate în dezvoltarea aterosclerozei (ATS). Indicii aterogenici: Indicele de risc Castelli I-CRI, Indicele de risc Castelli II-CRII, Indicele aterogenic –AI şi Coeficientul aterogenic-AC sunt predictori buni ai viitoarelor evenimente cardiovasculare. Scopul studiului a fost de a evalua profilul lipidic şi indicii aterogenici, la pacienţii senescenţi cu ATS carotidiană, în corelaţie cu HeartScore şi suprafaţa totală a ateroamelor. Au fost luaţi în studiu: grup cu ateroscleroză carotidiană -ATS1; grup cu ateroscleroză carotidiană cu grad avansat de stenoză-ATS2 vs. grupul de control-C, fără ateroame semnificative. Am obţinut valori ridicate ale colesterolului şi LDL-colesterol la ATS1 vs. C şi o scădere a valorilor HDL-colesterol la ATS2 vs. C. Mai mult, AI şi HeartScore sunt crescute în ATS2 vs. C. Pentru toate grupurile, AI are o valoare peste 0,24 ceea ce reprezintă un risc ridicat la toţi pacienţii incluşi în studiu. HeartScore indică un risc intermediar pentru ATS1 şi risc ridicat pentru ATS2. Ecuaţia de regresie liniară a relevat, pentru ATS1, o corelaţie semnificativ pozitivă între HeartScore şi AC, AI, CRI. În ceea ce priveşte ATS2 există o corelaţie semnificativ pozitivă între aria ateroamelor şi AC, CRI, CRII. AI poate contribui la valoarea predictivă/diagnostic mult mai bine decât lipidele individuale, ca marker de risc

cardiovascular. Toate aceste date subliniază faptul că indicii aterogenici sunt indicatori puternici ai riscului de boli cardiovasculare şi că există o corelaţie directă între HeartScore şi progresia ATS.
Cuvinte cheie: indici aterogenici, HeartScore, ateroscleroză

INTRODUCTION

Atherosclerosis (ATS) is a multifactorial complex disease and one of the leading causes of global morbidity and mortality. The process initiate early in life, progresses slowly and asymptomatically with aging, leading to atherosclerotic cardiovascular disease, adverse vascular events and eventually death. Clinical studies suggest that many inflammatory agents and innate immune pathways orchestrate the whole course of atherogenesis. Moreover, large cohort studies established some algorithms for predicting atherosclerosis [1,2,3].

According Kutuk et al. [1] lipid peroxidation and inflammation are cooperative events involved in atherosclerosis development and increased oxidative stress [2] may predict future events in patients with cardiovascular disease (CVD). A significant risk factor is low density lipoprotein-LDL and the protective one is high density lipoprotein-HDL [3]. High triglyceride (TG) level combined with low HDL-cholesterol or high LDL-cholesterol is associated with atherosclerosis, the build-up of fatty deposits in artery walls that increases the risk for heart attack and stroke.

The ratio of TG/HDL is a strong predictor of heart attack and a risk of developing myocardial infarction [4]. According Grover et al. [5], ratios LDL/HDL or TG/HDL are good predictors of future cardiovascular events and may serve as an indicator of atherogenic lipoprotein phenotype [6]. Atherogenic coefficient reflects atherogenic potential of full lipoprotein fractions spectrum [4, 7, 8] and atherogenic index is an indicator of atherosclerosis and is less susceptible to disease activity variation during large periods of time [9].

The need to estimate total cardiovascular risk in apparently healthy individuals has since 1994 been strongly advocated by the joint recommendations from The European Society of Cardiology, European Society of Hypertension, European Atherosclerosis Society and other societies [10,11,12]. HeartScore is aimed at supporting clinicians in optimising individual cardiovascular risk reduction and is the interactive version of SCORE - Systematic COronary Risk Evaluation - a cardiovascular disease risk assessment system initiated by the European Society of Cardiology, using data from 12 European cohort studies (N=205,178) covering a wide geographic spread of countries at different levels of cardiovascular risks [12]. This risk estimation is based on the following risk factors: gender, age, smoking, systolic blood pressure and total cholesterol [13]. The program chart shows absolute cardiovascular risk, and the contribution of modifiable risk factors to total risk in a chart of pie. The expected effect of intervention is calculated using large randomized clinical trials in hypertension and hypercholesterolemia. However, the program is designed so that it can be adapted to local conditions (national charts and translation), by National Societies of Cardiology [10-13].

The aim of present study was to assess lipid profile and atherogenic indices, in senescent patients with carotid atherosclerosis, in correlation with HeartScore and total atheromas area.

MATERIALS AND METHODS

The study included 52 senescent patients (over 70 years), men and women, from National Institute of Gerontology and Geriatrics „Ana Aslan" and divided into two groups as follows:

– group ATS1-with carotid atherosclerosis (n=25)

– group ATS2-with carotid atherosclerosis and advanced stenosis (n=12)

vs. control group C (n=15) without significant atheromas.

Patients (diabetes mellitus, acute and chronic inflammatory state, neoplasie were excluded) with significant atherosclerotic injury, evidenced by carotidian Doppler were compared with patients apparently healthy, without significant atherosclerosis injury. Written informed consent was obtained from all the study participants.

Doppler extracranian ultrasonography was performed with an ultrasound probe Interspec pencil Apogee Cx 5-MHz for spectral Doppler and sectorial pencil with variable frequency for echotomography.

Blood samples were taken by venopuncture into vacutainers without anticoagulant. The serum samples were separated from the clot by centrifugation 10 minutes at 1000x, within 4 hours of harvesting and then stored at -18 ° C until assayed. Lipid serum panel was assayed using commercial laboratory kits on automated analyzer (Konelab 301 SC).

From lipid serum panel we computed atherogenic indices:

Atherogenic Coefficient (AC) as ratio Total C-HDL/HDL

Castelli Risk Index I (CR I) as ratio Total C/HDL

Castelli Risk Index II (CR II) as ratio LDL/HDL

Atherogenic Index (AI) as log(TG/HDL)

AI values are associated with:

- low risk -0.3 ÷ 0.1
- medium risk 0.1 ÷ 0.24
- high risk above 0.24

Total cardiovascular risk was estimated with HeartScore, an interactive version of SCORE - Systematic COronary Risk Evaluation - a cardiovascular disease risk assessment system initiated by the European Society of Cardiology [12].

The HeartScore risk was divided into three subclasses according to the various algorithms [12]:

- low risk (HeartScore < 2%),
- intermediate risk (HeartScore 2% but < 5%) and
- high risk (HeartScore > 5%)

Data were collected and statistically analyzed with the use of the SPSS program for Windows. A Pearson test was used to compare categorical variables. For quantitative values, results were expressed as means ± S.D. Statistical analyses were done by Student's "t" test and $p<0.05$ was considered to be statistically significant. The relationship between HeartScore, atheroms area and atherogenic indices was assessed using a linear regression model.

RESULTS AND DISCUSSIONS

Quantitative and qualitative changes in lipid profile leads to dyslipidemia which is the major promoter of atherosclerosis. Combined hyperlipidemia and simple hypercholesterolemia, in which the primary abnormality was elevated LDL-cholesterol, were associated with increased subclinical ATS in both carotid and coronary arteries in patients with CVD, according to Yang et al. [14].

Our study revealed increased values of cholesterol (249.96 ± 50.14 vs. 235.26 ± 34.27) and LDL-cholesterol (154.48±45.48 vs. 143.36±25.15) at ATS1 vs. control and decrease HDL-cholesterol levels (43.81±8.54 vs. 52.22±17.82) at ATS2 vs. control group (Tab. I). Moreover, atherogenic index and HeartScore are elevated in ATS2 vs. control group (Tab. II).

Tab. I Serum lipid profile in ATS patients vs. Controls

	ATS 1	ATS 2	Control
Age (years)	76.48±9.17	69.58±8.78	74.33±11.17
Cholesterol (mg/dl)	249.96±50.14*	206.58±36.96**	235.26±34.27
Triglycerides (mg/dl)	160.8±99.49	189.08±47.53	165.46±96.68
HDL-Cholesterol (mg/dl)	52.12±10.64^{t}	43.81±8.54	52.22±17.82
LDL-Cholesterol (mg/dl)	154.48±45.48^{tt}	128.11±26.95	143.36±25.15

Results are presented as means±S.D.; $p^{*}<0.001$ vs. ATS2, $p^{**}<0.01$ vs. C, $p^{t}<0.005$ vs. ATS2, $p^{tt}<0.01$ vs. ATS2

It is indicated that non-HDL cholesterol and lipid ratios, including CRI and CRII, are CVD risk indicators with better predictive assessment for atherosclerotic progression or regression compared with conventional lipid profile [14, 15].

Tab. II Atherogenic indices, HeartScore and atheromas area in ATS patients vs. Control

	ATS 1	ATS 2	Control
Atherogenic coefficient	4.01±1.61	3.82±1.09	4.13±3.09
Castelli Risk Index I	5.01±1.61	4.82±1.09	5.13±3.09
Castelli Risk Index II	3.11±1.24	3±0.77	3.14±2.16
Atherogenic index	0.44 ± 0.3^{t}	0.62 ± 0.15^{tt}	0.45±0.36
HeartScore	$3.96\pm1.54^{**}$	5.25±1.71	4.26±2.81
Total atheromas area (mm^2)	$0.13\pm0.12^{*}$	38.43±25.60	non-disclosure

Results are presented as means±S.D.; $p^{*}<0.0001$ vs. ATS2, $p^{**}<0.01$ vs. ATS2, $p^{t}<0.01$ vs. ATS2, $p^{tt}<0.05$vs. C

For all groups (Tab. II), AI has a value above 0.24 indicating a high risk in all patients included in the study. This clearly suggests that atherogenic indices have more significant predictive and prognostic value than lipid parameters, including medication management.

From our data (Tab. II) HeartScore indicated an intermediate risk for ATS1 and a high risk for ATS2, therefore there is a direct correlation between HeartScore and atherosclerosis progression. Furthermore, linear regression equation revealed a positive significant correlation between HeartScore and atherogenic indices: AC (r=0.514; p<0.01), AI (r=0.587; p<0.005) and CRI (r=0.514; p<0.01) at ATS1 (Fig.1, Fig.2, and Fig.3).

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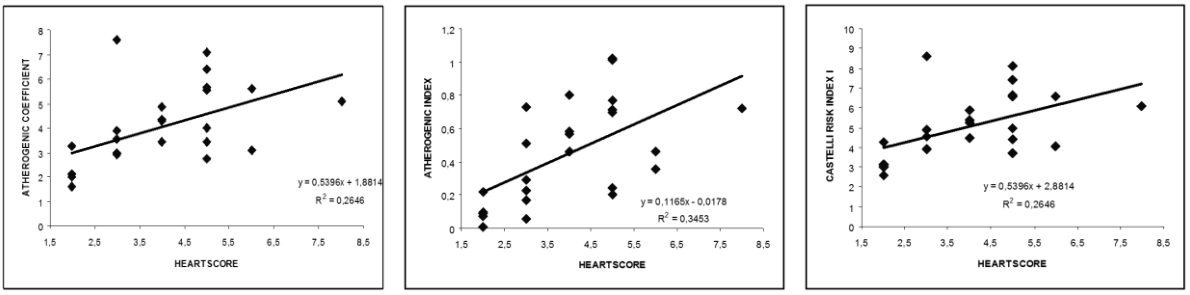

Fig.1-3 Correlation between HeartScore and Atherogenic Coefficient, Atherogenic Index, Castelli Risk Index I at ATS1

Curve fitting was by linear regression; r = correlation coefficient

As shown in Fig.4, Fig.5, Fig.6, linear regression equation revealed a positive significant correlation between atheromas area and atherogenic indices: AC (r=0.667; p<0.01), CRI (r=0.667; p<0.01) and CRII (r=0.666; p<0.01) at ATS2.

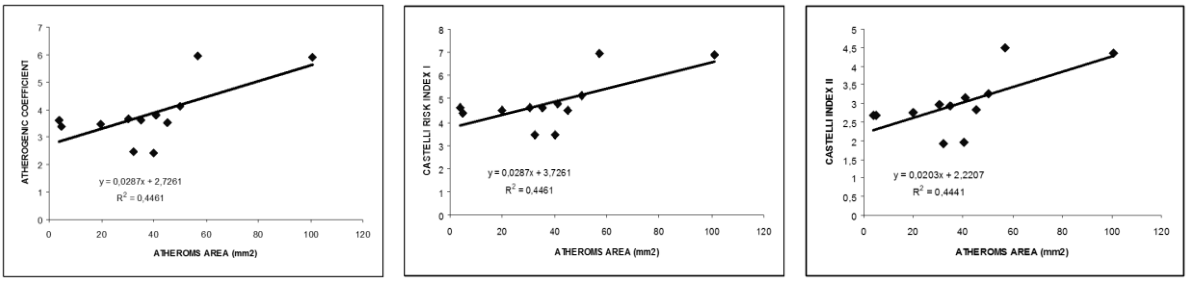

Fig.4-6 Correlation between atheromas area and Atherogenic Coefficient, Castelli Risk Index I, Castelli Risk Index II at ATS2

Curve fitting was by linear regression; r = correlation coefficient

Yildiz et al. [16] found too a significant correlation between AI and increased carotid intima-media thickness in the patient group and it was found to show a correlation with a greater number of risk factors. Thus, AI can be regarded as a good predictor of CVD.

CONCLUSIONS

- Atherogenic indices are strong indicators of CVD risk, with better predictive assessment for ATS progression compared with conventional lipid profile;
- There is a direct correlation between HeartScore and ATS progression;
- AI and HeartScore might be used in diagnosis of subclinical ATS and possibly other long/short-term CVD events.

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IL-1β IN ELDERLY PATIENTS WITH TYPE 2 DIABETES

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Abstract. Diabetes mellitus includes a variety of syndromes with different etiologies characterized mainly by hyperglycemia. Proinflammatory cytokines secreted by adipose tissue and other tissues play an important role in this process and can cause insulin dysfunction in adipose tissue, skeletal muscle and liver by inhibiting insulin signal transduction**.** Interleukin-1β (IL-1β), a major proinflammatory cytokine could promote beta-cell destruction and alter insulin sensitivity. Aims of this study was to determine changes in serum levels of IL-1β in elderly patients with type 2 diabetes compared to a control group. Quantitative determination of IL-1β was performed by an immunological sandwich ELISA method. Our results showed an increase of IL-1β levels at one group of patients with type 2 diabetes compared with a control group (7.829 ± 16.50 vs 4.628 ± 12.07 pg / mL serum). In conclusion, serum IL-1β levels are elevated in individuals with diabetes associated with obesity, indicating that IL-1β, as a proinflammatory cytokine, plays an important role in the pathophysiology of type 2 diabetes and pancreatic beta cell functions.
Key words: interleukin-1 beta, type 2 diabetes, elderly

IL-1β LA PACIENŢII VÂRSTNICI CU DIABET ZAHARAT DE TIP 2

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Rezumat. Diabetul zaharat include o varietate de sindroame cu diferite etiologii caracterizate în principal de hiperglicemie. Citokinele proinflamatorii secretate de ţesutul adipos şi alte ţesuturi joacă un rol important în acest proces şi pot provoca disfuncţii ale insulinei în ţesutul adipos, muşchiul scheletic şi ficat prin inhibarea transducţiei semnalului de insulină. Interleukina-1β (IL-1β), o citokină proinflamatorie majoră, poate stimula distrugerea celulelor beta şi poate altera sensibilitatea la insulină. Scopul acestui studiu a fost de a determina modificările nivelurilor serice de IL-1β la pacienţii vârstnici cu diabet zaharat de tip 2, comparativ cu un grup de control. Determinarea cantitativă a IL-1β a fost efectuată printr-o metodă imunoenzimatică ELISA. Rezultatele noastre au arătat o creştere a nivelurilor de IL-1β la grupul pacienţilor cu diabet zaharat de tip 2, comparativ cu grupul de control (7.829 ± 16.50 vs 4.628 ± 12.07 pg/mL ser). În concluzie, nivelurile serice ale IL-1β sunt crescute la persoanele cu diabet zaharat, ceea ce indică faptul că IL-1β, ca citokină proinflamatorie, joacă un rol important în fiziopatologia diabetului de tip 2 şi a funcţiilor celulelor beta pancreatice.
Cuvinte cheie: interleukina-1 beta, diabet zaharat tip 2, vârstnici

INTRODUCTION

Diabetes mellitus includes a variety of syndromes with different etiologies characterized mainly by hyperglycemia. The distinctive pathophysiological signs of type 2 diabetes are increased tissue insulin resistance, accompanied by decreased insulin secretion, and pancreatic beta cell dysfunction [1].

Lack of tissue insulin response is most likely due to alteration of the insulin receptor on the cell membrane, while beta cell dysfunction is mainly destroyed by autoimmune-mediated apoptosis, which

leads to a decrease in insulin production [2].
Proinflammatory cytokines secreted by adipose tissue and other tissues play an important role in this process and can cause insulin dysfunction in adipose tissue, skeletal muscle and liver by inhibiting insulin signal transduction [3].
Interleukin-1β (IL-1β), a major proinflammatory cytokine could promote beta-cell destruction and alter insulin sensitivity [4]. The major source of IL-1 cytokines is the mononuclear phagocytic cell line (macrophage), although it can also be synthesized in many other cells (endothelial cells, keratinocytes, osteoblasts, neutrophils, glial cells). Stimulants of IL-1 secretion are endotoxins, other cytokines, microorganisms, various antigens [5].
A number of studies had shown that IL-1β plays a role in normal homeostasis and in the inflammatory response which is deemed to be responsible for the development of major chronic diseases that are highly prevalent in the elderly, including autoimmune diseases such as inflammatory intestinal disease and type 1 diabetes, rheumatoid arthritis, and diseases associated with metabolic syndrome such as atherosclerosis, chronic heart failure and type 2 diabetes [6, 7].
The present study aims to determine changes in serum levels of IL-1β in elderly patients with type 2 diabetes compared to a control group.

MATERIALS AND METHODS

Studies were carried out in 75 patients (men and women) aged between 50 – 85 years, hospitalized at the "Ana Aslan" National Institute of Gerontology and Geriatrics in according to an inclusion / exclusion protocol in agreement with physicians. All the subjects gave informed consent to participate in the study.
Selected patients were divided in two study groups:
a) a control group (n = 28 apparently healthy subjects)
b) a type 2 diabetes mellitus group (n = 47)
For all patients studied, were determined biochemical and hematological parameters.

Evaluation of biochemical and hematological parameters

Venous blood samples were obtained from patients after 12 hours of fasting and serum was collected after 20 minutes of centrifugation at 1000 x g and stored at -70 ° C until use. Serum determinations of biochemical parameters: blood glucose, total cholesterol (TC), high density lipoproteins (HDL-C), low density lipoproteins (LDL-C), triglycerides (Tg) were performed using standardized methods with Konelab 301 SC autoanalyzer. Hematological parameters (hemoglobin, hematocrit, leukocyte count, lymphocytes, platelets, erythrocyte sedimentation rate) were also determined by standardized methods with Celltac F MEK-822K specific reagents.
The atherogenic index (IA) is based on the ratio of two major parameters, Tg and HDL-cholesterol; both being considered independent risk factors for cardiovascular disease [8].
AI values are associated with:
- low risk -0.3÷0.1
- medium risk 0.1÷0.24
- high risk >0.24

IL-1β determination

Serum IL-1β was determined by ELISA method (Enzyme-linked Immunosorbent Assay) for quantitative detection of human IL-1β, using a R&D Systems kit. Color change is detected with a microplate reader at 450 nm wavelength and the results are expressed in pg / mL. The minimum detectable dose of IL-1β is typically less than 1 pg/mL.

Anthropometric measurements

Weight and height of the participants were measured when the participant had thin clothes on and was wearing no shoes by using the standard scales. Body mass index (BMI) was calculated for each individual by division of body weight (kg) by height (m^2).

Blood pressure was measured using a tensiometer, with the patient rested for 5 min in the seated position, arm supported and using an appropriate-sized cuff.

Statistical analysis

All values are represented as mean ± SD. Statistical analysis was done by using the Student "t" test (EXCEL 7.0 and SPSS 8.0 Microsoft Software). A p-value less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSIONS

For all patients under study, were determined some biochemical and hematological parameters.

Tab. I Biochemical and clinical parameters in the studied groups

Biochemical and clinical parameters	**Control group n = 28**	**Type 2 diabetes group n = 47**
Glucose (mg/dL)	91.67±6.56	147.04±54.18
Total cholesterol (mg/dL)	221.64±34.91	241.13±40.09
HDL-cholesterol (mg/dL)	56.17±15.49	43.87±12.47
LDL-cholesterol (mg/dL)	129.28±38.87	142.77±35.72
Triglycerides (mg/dL)	118±38.26	188.89±92.17
BMI (kg/m2)	22.97±10.69	31.48±9.52
Atherogenic index	0.311±0.22	0.60±0.28
Systolic blood pressure (mmHg)	12.76±1.68	13.38±3.95
Diastolic blood pressure (mmHg)	7.64±0.76	7.35±2.19

Values are presented as mean ± D.S.

Tab. II Hematological parameters in the studied groups

Hematological parameters	**Control group n = 28**	**Type 2 diabetes group n = 47**
Hemoglobin (g/dL)	13.24 ± 1	13.29 ± 1.07
Hematocrit (%)	39.84 ± 3.02	40.09 ± 2.91
White Blood Cell (10^3/µL)	5742.86 ± 1252.09	7290.91 ± 1504.85
Lymphocytes (%)	30.98 ± 8.95	28.91 ± 7.43
Platelets (10^3/µL)	252428.6 ± 53259.3	259090.9 ± 54590.6
Erythrocyte Sedimentation Rate (mm/hr)	10.71 ± 6.29	18.09 ± 10.74

Values are presented as mean ± D.S.

Statistical analysis of our study showed that are not significant differences between the control group and diabetes group of patients, regarding their serum levels of lipidic and lipoproteic parameters: total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides (Tab. I) as well as between their hematological parameters (Tab. II).

From atherogenic index point of view of, we observed that the values are higher than 0.24, indicating an increased risk of cardiovascular disease for all patients included in the study, especially in patients with diabetes.

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Tab. III Serum levels of IL-1β in the studied groups

	IL-1β (pg/mL)
Control group	4.628 ± 12.07
Type 2 diabetes group	7.829 ± 16.50
Presenescent group (50-65 years)	4.85 ± 10.13
Senescent group (66-85 years)	8.46 ± 18.61

Values are presented as mean ± D.S.

Research data pointed out that serum IL-1β levels were higher in diabetic patients compared to the control group, as well as in the senescent group compared to presenescent group (Tab. III).

Maedler et al. have shown that human β cells themselves are capable of producing IL-1β independently of any viral infection or immune mediated process, in response to glucose. This indicates that IL-1β–producing β cells were also detected in tissue sections of type 2 diabetic patients [9].

The positive relationship between IL-1β and glucose levels and glycosylated hemoglobin (HbA1c) in diabetic patients associated with obesity is another observation in this study, which explains the role of these inflammatory cytokines in the prevalence of diabetes and the determination of type 2 diabetes mellitus (Fig. 1).

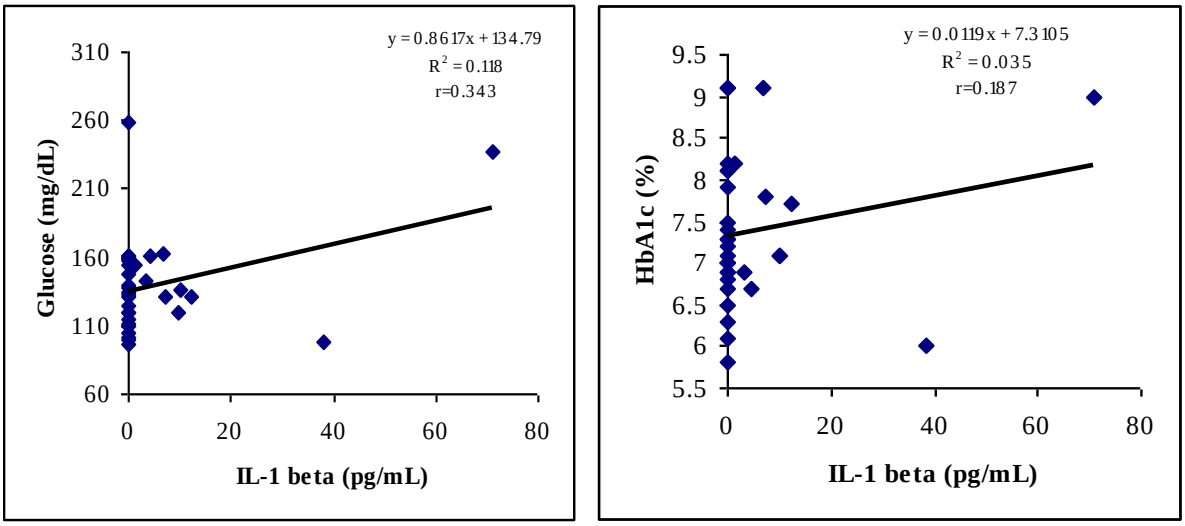

Fig. 1 Correlation between IL-1β with glycemia respectively glycosylated hemoglobin, in the diabetes group with obesity
Y = the linear regression equation; r = correlation coefficient

Generally, adipose tissue accumulation, increasing body fat percentage, especially abdominal obesity, leads to increased inflammatory cytokine levels and decreased anti-inflammatory markers, paving the way for chronic inflammatory diseases. Thus, it has been observed that in patients with obesity who also suffer from diabetes or cardiovascular disease, in addition to obesity, the type of disease also affects the level of inflammation or anti-inflammatory mediators [10].

Therefore, some studies reported an increase in the number of inflammatory cytokines in obese patients compared with normal people [11]. Also, previous studies have described a positive association between IL-1β gene polymorphism and obesity, suggesting functional effects on fat mass, fat metabolism and body mass [12].

In addition, our study found a correlation between IL-1β and lipid profile (TC, HDL-C, LDL-C) and also, with atherogenic index in diabetes group with obesity, but is no statistically significant (Fig. 2).

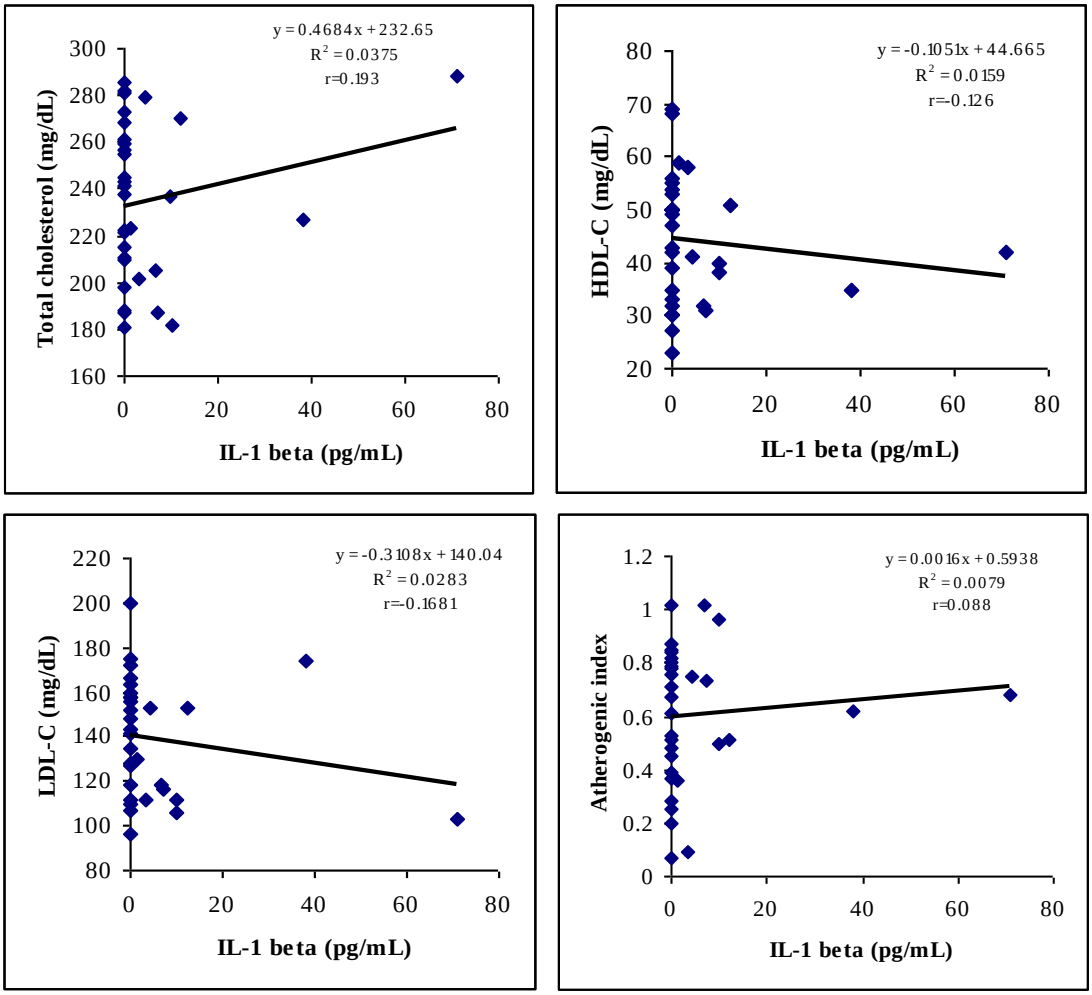

Fig. 2 Correlation between IL-1β with lipid profile (TC, HDL-C, LDL-C) respectively atherogenic index in the diabetes group with obesity
Y = the linear regression equation; r = correlation coefficient

Diabetes is a disease related to obesity and a risk factor for cardiovascular disease which is also associated with atherosclerosis. Thus, studies have shown that IL-1β plays an important role in the metabolism of lipids by regulating insulin levels and lipase activity under physiological conditions [13].

CONCLUSIONS

In conclusion, serum IL-1β levels are elevated in individuals with diabetes associated with obesity, indicating that IL-1β, as a proinflammatory cytokine, plays an important role in the pathophysiology of type 2 diabetes and pancreatic beta cell functions. Interaction mechanisms between them are still unknown, so additional studies are needed in this area..

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PREVALENT CLUSTERS OF COMPONENTS OF METABOLIC SYNDROME IN ELDERLY WOMEN PATIENTS

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Abstract. This work has attempted to show in a group of elderly women inpatients, prevalent clusters of concomitant components of the metabolic syndrome as found out and to a certain extent, dissimilar from combinations of risk factors according to definitions of the metabolic syndrome. Data were collected for this retrospective study out of 86 medical records of women patients aged 68±5 years who were admitted at Ana Aslan NIGG between Feb 2011-July 2011. There were complete data for 67 of these women patients. 44 (67%) of these patients received anti-hypertensive drugs and 43 (65%) of them had clusters of two and three risk factors of the metabolic syndrome. Regarding dyslipidemia as risk factor, results pointed out in a majority of these patients either only elevated triglycerides levels or only low HDL-C. Only four patients (5.9%) had four components of the metabolic syndrome. Conclusion: a most prevalent clustering of risk factors among these patients with metabolic syndrome was that combining hypertension and obesity. More thorough investigations of the cardiovascular disease in elderly women patients with hypertension and obesity and those with hypertension and prediabetes are needed.
Key words: elderly women, metabolic syndrome, risk factors clustering

COMBINAŢII PREVALENTE DE FACTORI DE RISC AI SINDROMULUI METABOLIC LA PACIENTE VÂRSTNICE

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Rezumat. Lucrarea încearcă să arate, în cazul unui grup de paciente vârstnice, asocieri prevalente de componente concomitente ale sindromului metabolic, diferite într-o anumită măsură, de combinaţiile de factori de risc conforme cu definiţiile sindromului metabolic. Pentru prezentul studiu retrospectiv, datele au fost colectate din 86 foi de observaţii ale unor paciente vârstnice, vârsta medie 68±5 ani internate la INGG Ana Aslan între februarie şi iulie 2011. Datele au fost complete în cazul unui număr de 67 paciente. 44 dintre aceste vârstnice (67%) primeau medicaţie antihipertensivă, iar 43 dintre ele (65%) aveau asocieri de doi şi trei factori de risc ai sindromului metabolic. Privind dislipidemia ca factor de risc, rezultatele au evidenţiat în cazul unei majorităţi a pacientelor fie numai trigliceride crescute, fie numai HDL-C scăzut. Numai patru dintre paciente (5.9%) au avut cele patru componente de sindrom metabolic. Concluzie: o asociere prevalentă de factori de risc

ai sindromului metabolic la aceste paciente vârstnice, este cea care combină hipertensiunea şi obezitatea. Investigaţii cardiovasculare mai complexe sunt necesare în special pentru pacientele vârstnice hipertensive cu obezitate sau hipertensive cu prediabet.
Cuvinte cheie: vârstnice, sindrom metabolic, asociere factori de risc

INTRODUCTION

Over the years the metabolic syndrome (METSYN) known as „dyslipidemic hypertension, deadly quartet, insulin resistance syndrome and hazardous waist" has been regarded more as a medical concept and less as a diagnosis [1]. Metabolic syndrome is identified in patients based on presence of insulin resistance, systolic blood pressure (BP) higher than 140 mm Hg and diastolic BP higher than 90 mm Hg, plasma triglycerides (TG) higher than 150 mg/dl, HDL-C less than 35 mg/dl in men and less than 39 mg/dl in women and central obesity [2]. The definition of the metabolic syndrome asserts that three out of the five components of the metabolic syndrome must be present in a patient to confirm that he has the syndrome [3]. Despite controversies about definitions of the metabolic syndrome, the increased risks for cardiovascular disease and type 2 diabetes mellitus (DB) progressions have been acknowledged for patients with this syndrome [4,5,6,7]. Modalities in which cardiovascular risk changes depending on concomitant presence of certain metabolic syndrome components have been also shown. Aijaz B [8] pointed out increase in left ventricular mass and its dysfunction in patients having metabolic syndrome risk factors and as well investigations have noted in patients with components of metabolic syndrome the increased risk of death from heart failure [8,9].

In contrast, researches regarding patients with rheumatoid arthritis in whom cardiovascular risk factors were maintained within the goal range, showed that presence of metabolic syndrome components did not have influence on progression of the coronary heart disease (a fact pointed out by unchanged calcification scores for coronary arteries [10]. Also, new markers of cardiovascular disease appeared to be more predictive for the disease onset than some metabolic syndrome risk factors [11].

This work aims to show in a population sample of elderly women patients, clusters of concomitant components of the metabolic syndrome as found out and somewhat dissimilar from clustering of risk factors according to definitions of metabolic syndrome.

MATERIALS AND METHODS

Out of 86 medical records data could be collected for 67 women inpatients (complete data in their medical records), mean age 68$\pm$5 years who were admitted at "Ana Aslan"National Institute of Gerontology and Geriatrics between Feb 2011-June 2011.

Subjects gave their written informed consent for their data to be included in the study. Patients with active liver disease, hematological diseases and cancer were excluded from the study.

Blood pressure was measured using mercury sphygmomanometers with cuff placed on the upper arm. BMI, which is ratio weight/height (kg/m2) remains the measurement used ubiquitously to identify obesity [12]. Depending on BMI values patients may be underweight (BMI less than 18.50) or patients with thinness varying from severe to mild thinness (BMI 16.00-18.49) or normal weight patients (18.50-24.99) or overweight patients with pre-obesity (BMI 25.00-29.99) and patients with obesity (BMI higher than 30).

There was a lack of data on glycated hemoglobin (HbA1c) in patients with fasting glycemia higher than 100mg/dl and nor were data about impaired glucose tolerance expressed as 2 hours plasma glucose after ingestion of an oral dose of 75g glucose. Levels of glycated hemoglobin identify normal patients (HbA1c below 42 mmol/mol) those with prediabetes (HbA1c 42-47mmol/mol) and patients with type 2 diabetes (Hb A1c 48mmol/mol and above on two separate tests) [13]. According to specialized literature, prediabetes is indicated by both plasma glucose levels higher than 100mg/dl and 2 hours plasma sugar levels between 140 and 199mg/dl [14].

RESULTS AND DISCUSSIONS

Clinical and biochemical parameters were shown in Tab. I.

Tab. I Main features in elderly female patients (n=66)

BMI (kg/m^2)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Glycemia (mg/dl)	Total cholesterol (mg/dl)	HDL-C (mg/dl)	Triglycerides (mg/dl)	LDL-C (mg/dl)
31.6±6.2	147±10	85±12	101±21	223±59	53±13	134±38	143±31

Results are presented as mean ± S.D.

44 (67%) of these patients had hypertension and received anti-hypertensive drugs and 43 (65%) of them had various combinations of metabolic syndrome components (Tab. II) of them had clusters of two and three risk factors of the metabolic syndrome. Nine of these patients (13.4%) had type 2 diabetes mellitus. Regarding dyslipidemia as risk factor, results pointed out in a majority of these patients either only TG higher than 150 mg/dl or only HDL-C lower than 49 mg/dl. Rarely had we dyslipidemia in accordance with the the metabolic syndrome definition for atherogenic dyslipidemia, namely presence of both low HDL-C and elevated TG levels. Only four patients (5.9%) had four components of the metabolic syndrome, according to the definition for the syndrome. A most prevalent combination of risk factors was that of hypertension and obesity (BMI higher than 30) in 36 (53.7%) of these elderly women patients.

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Tab. II Combinations of metabolic syndrome risk factors in elderly female patients (n=66)

METSYN Components	Number of patients
HBP + obesity + higher C + higher TG	24
HBP + obesity +low HDL-C+ high TG	12
HBP + obesity + type 2 DB	7
HBP + obesity + type 2 DB + low HDL-C+ high TG	2
HBP + obesity + hypergly + low HDL-C + high TG	2
HBP + obesity + hypergly	5
Obesity + hypergly + high TG	2
Obesity + high TG	7
Obesity + low HDL-C	5
	Total 66 patients

Abbreviations: METSYN= metabolic syndrome; HBP= high blood pressure; DB= type 2 diabetes mellitus; hypergly= hyperglycemia; C= total cholesterol

In Tab. III we showed for this group of elderly women prevalence of each component of the metabolic syndrome. In these women patients there were either high TG or low HDL-C.

Tab. III Prevalence for each risk factor of the metabolic syndrome in elderly female patients (n=66)

METSYN	Number of patients
HBP	52 (78%)
Obesity	42 (63%)
DB (higher than 126 mg/dl)	9 (13.6%)
Hyperglycemia	9 (13.6%)
Low HDL-C	9 (13.6%)
High TG	9 (13.6%)

Abbreviations: METSYN =.metabolic syndrome; HBP= high blood pressure; DB= type 2 diabetes mellitus

We found out in this study a predominant share of 63% elderly women with obesity. Another 27 % of these women patients had abnormalities of glucose metabolism (hyperglycemia and type 2 DB). So, as regards risk factors of metabolic syndrome, hypertension, obesity and hyperglycemia were the most frequent among these patients. Because of the majority of these patients having hypertension, we may say that the other metabolic syndrome components they had may have increased considerably their cardiovascular risk. Also, average body mass index higher than 30 may have been a main factor leading to insulin resistance and prediabetes [15].

In specialized literature there were attempts to add to the metabolic syndrome risk factors such as the uric acid [16, 17, 18]. However, the cause of elevations of uric acid levels may be for example, the inappropriate treatment with diuretics. Recent discussions concentrated nevertheless, on the need to specify out of routine measurements, which ones are more appropriate in insulin resistance, pro-inflammatory and pro-thrombotic states of the metabolic syndrome. Yet no consensus on inclusions of high sensitivity C reactive protein (hsCRP) and plasminogen activator inhibitor-1 (PAI-1) in the metabolic syndrome cluster has been reached. Published data showed that weight loss can decrease both serum levels of hs CRP and PAI-1. It was as well mentioned that measurement of hsCRP should be limited to patients who, according to their Framingham scores, were at an intermediate risk for coronary heart disease [2].

Studies have pointed out that pathogenesis of cardiovascular disease and that of type 2 diabetes mellitus are much more complex than as determined by metabolic syndrome risk factors [19]. In this sense, Krans HMJ [20] mentioned that „ in addition to central obesity and insulin resistance, the following factors all contribute to diabetes mellitus and cardiovascular diseases: activation of the immune system; disordered hypothalamic-pititary-adrenal axis; altered glucocorticoid action: involvement of cytokines, hormones and other molecules from adipose tissue; prenatal and early life influences; multiple gene combinations, stress" and abnormalities of coagulation. So, „the metabolic syndrome should only be considered as a pre-morbid condition and should exclude persons with established diabetes or known cardiovascular diseases".

Limitations

Lack of data on waist circumference, which is the reason for not describing phenotypes in these elderly women. No data on possibly administered lipid lowering compounds, drug treatment (statins) and lifestyles of these subjects.

CONCLUSIONS

The most prevalent cluster of metabolic syndrome risk factors was that combining obesity and hypertension. More thorough

investigations of the cardiovascular disease in elderly women patients with hypertension and BMI higher than 30 and in those with hypertension and prediabetes are needed.

Conflicts of interest

The authors declare no conflicts of interest.

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UPDATES ON SERUM PROTEINS ELECTROPHORESIS

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Abstract. Serum protein electrophoresis is a routine test, usually performed using agarose gel as support. Despite ready to-use commercial reagent and semi-automated systems, this technique remains labour intensive limited by multiple interferences. Capillary electrophoresis appears to be a viable alternative to standard electrophoresis, especially because the most frequent interferences in agarose gel electrophoresis (hemolysis, jaundice and turbidity, as well as point of application artefacts and weak monoclonal bands) had no effects on capillary electrophoresis electrophoregrams. The analysis of low protein fluids (cerebrospinal fluid and urine) and more specialized analysis such as for glycated hemoglobin Hb Alc and transferin sialoforms available on multicapillary system remain the interesting perspective for capillary techniques. Although not currently available, the capillary electrophoresis promises to be a rapid, inexpensive and more sensitive technique than agarose gel electrophoresis.
Key words: capillary electrophoresis, serum proteins, interferences, artifacts

NOUTĂŢI ÎN ELECTROFOREZA PROTEINELOR SERICE

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Rezumat. Electroforeza proteinelor serice este o analiză de rutină, gelul de agaroză fiind cel mai utilizat suport electroforetic. În pofida automatizării sistemelor electroforetice şi a disponibilităţii pe piaţă a reactivilor deja pregătiţi pentru utilizare, aceast tehnică este relativ laborioasă şi supusă unor interferenţe multiple. Electroforeza capilară este o alternativă viabilă la electroforeza clasică, în special datorită faptului ca cele mai frecvente interferenţe cunoscute pentru tehnicile electroforetice (hemoliza, icterul şi lactescenţa serului, precum şi artefactele legate de punctul de aplicare a probelor şi prezenţa componentelor monoclonale de concentraţie scăzută) rămân fără efect asupra electroforezei capilare. Separarea electroforetică a proteinelor din fluidele hipoproteice (lichid cefalorahidian şi urină) precum şi determinarea cantitativă a hemoglobinei glicozilate şi analiza sialoformelor transferinei în sistem multicapilar constituie perspective importante în dezvoltarea tehnicilor electroforetice în sistem Capillarys. Desi puţin accesibilă în prezent, electroforeza capilară se impune ca o metodă de viitor, rapidă şi mult mai sensibilă decât electroforeza în gel de agaroză.
Cuvinte cheie: electroforeză capilară, proteine serice, interferenţe, artefacte

INTRODUCTION

Electrophoresis is a key assessment within the range of present biochemical investigations while progressing from "special" investigation to a "routine" one. At present there are three major areas of applications for electrophoretic separations:

- as means to confirm a diagnosis;
- as screening test for a number of individuals with a specific pathology in

order to evaluate progression of pathology and efficacy of treatment;

- as means of mandatory investigation in healthy subjects to evaluate risk of disease and early detect point in time when metabolic and immunological imbalances occur [1].

Serum proteins, urine proteins, low-protein fluids, hemoglobin, lipoproteins, isoenzymes were enumerated among possible biochemical parameters to investigate by electrophoresis.

At present two types of electrophoresis methods are used: standard agarose gel electrophoresis (AGE) and capillary electrophoresis (CE).

Depending on equipment and techniques utilized, reagent producing companies designed complex programs to investigate various biochemical parameters by use of electrophoresis in gel.

Agarose Gel Electrophoresis is a separation method conducted in Hyrys-Hydrasys SEBIA semi-automated system, at alkaline pH (Tab. I). Proteins were colored with amido-black, excess of colored compound was removed using an acid solution. Migration, staining, washing and drying were fully automated, while samples and anti-sera were transferred manually.

Tab. I Classical electrophoresis

Study parameter	Separated fractions	Purpose
Serum proteins	5 or 6 (pH dependent separation): albumin, α1, α2, β (β1-β2), γ globulins	-quantitative assessment of separated fractions -identification of monoclonal bands
Lipoproteins	-3(beta, pre-beta and alfa-lipoproteins) -screening of Lp(a)	- for inclusion in a type of dyslipidemia - identification of pro- and non-atherogenic risk factors
Apolipoproteins	-apolipoproteins AIB -apolipoprotein AI -apolipoprotein CIII -apolipoprotein E -Lp(a) -evaluation of ratio LDL/HDL cholesterol	- identification of pro- and non-atherogenic risk factors
Haemoglobins	-separation in an alkaline medium (Hb A0, Hb F, Hb A2) -separation in an acid medium (Hb S, C, D, E)	-identification of quantitative abnormalities (thalassemia) - identification of qualitative abnormalities
Glycosylated Haemoglobin	Hb A0, Hb A1 a+b, Hb A1c	-quantitative assessment of Hb A1c aiming to specify onset of diabetes and evaluate efficacy of treatment
Immunofixation	-Serum immunoglobulins (Ig G, A, M, lanţuri usoare K, L) -Urinary immunoglobulins -Bence Jones Proteins	-identification and characterization of monoclonal gammopathies
Urinary proteins	-High resolution electrophoresis -SDS-gel electrophoresis (without changing concentrations)	-establishing type of proteinuria (mixed, tubular, glomerular) -identification of free and/or bound light chains
LCR proteins	-identification of oligoclonal bands (without changing concentrations)	-evidence of Ig intrathecal synthesis -diagnosis and prognosis of multiple sclerosis
Proteins from other biological fluids (saliva, tears, amniotic, synovial, seminal fluids)	-high resolution electrophoresis -SDS-gel electroforesis	-assessment of specific proteins (lactoferrin, lysozyme, albumin, immunoglobulins)
Izoenzymes	CK (CKMM, CKBB, CKMB, macro CK I şi II) LDH (LDH1, LDH2, LDH3, LDH4, LDH5) PAL (bone, hepatic, intestinal, placenta isoenzymes)	-establishing diagnosis which is difficult to do through other investigations.

Capillary Electrophoresis, the most modern method, is an intermediary between classical electrophoresis with electrophoretic zones and various support media and liquid chromatography (Tab. II). This type of electrophoresis was developed in parallel with the classical one, the capillary electrophoresis providing the advantage of being fully automated from identification of patients with the bar code to conducting pre- and post- separation stages when using the Capillarys SEBIA system and thus, full removing human errors.

Capillary electrophoresis allows separation of molecules with electric charge depending on their mobility in a buffer with a specific pH and the electroosmotic flow. Separation takes place in capillaries made of silicium, with a diameter less than 100 microm, filled with buffer containing various electrolytes. Injection of samples (previously diluted in buffer) is performed through aspiration at the anode. Separation is conducted by power supply at the end of capillaries. Density is measured in fractions at the cathode at wavelengths specific of type of protein mixture, which is separated. At the end, capillaries are washed with a washing solutions and a buffer solution.

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Tab. II Capillary electroforesis

Study parameter	Separated fractions	Purpose
Serum proteins	5 or 6 (pH dependent separation) albumin, α1, α2, β (β1-β2), γ globulins	-quantitative assessment of separated fractions -monoclonal bands identification
Serum proteins	-high resolution electrophoresis– 8 fractions: - albumin - β1 globulins - β2 globulins - γ globulins - α2 macroglobulin - α1 glicoprotein acidă - α1 antitrypsin - haptoglobin	-identification of study-fractions
Urinary proteins	-SDS-gel electrophoresis (without changing concentrations) -high resolution electrophoresis	-establishing type of proteinuria (mixed, tubular, glomerular) -identification of free and/ or bound light chains
Haemoglobins	-separation in an alkaline medium (Hb A0, Hb F, Hb A2)	-identification of quantitative abnormalities (thalassemia)
CDT (Carbohydrate deficient transferrin)	5 fractions: Asialo-, disialo-, trisialo-, tetrasialo-, pentasialo-transferrin	-confirming acute and chronic alcohol consumptions -screening of persons assumed as chronically abusing alcohol -identification of chronic abusers among persons who had traumatic (events) in order to prevent post-traumatic complications -identification of patients with hepatic diseases of ethylic etiology -early detection of alcohol abuse and predisposition to abuse -long term screening for relapse at patients under treatment -identification of gene variants of transferrin -diagnosis of congenital glycosylation disorders
Immunotyping	Serum immunoglobulins Ig G, A, M, light chains, K, L	-identification and characterization of monoclonal gammopathies

Clear advantages of the capillary electrophoresis were pointed out by comparing stages of the two electrophoretic methods:

- higher degrees of resolution, specificity and sensitivity for capillary electrophoresis;
- speed during performing enabled by the possibility to simultaneously analyze from 10 samples (in immuno-phenotyping) to 80 samples per hour (serum proteins). In terms of time, we note the 20 minutes for standard electrophoresis in agarose gel vs 120 seconds for capillary electrophoresis;
- total traceability from primary sample to results and for the reagents' lot;
- implementation of the program for quality control in three steps (stages) allowing the possibility to statistically analyze results (Levey-Jennings curve) and programs to transfer results for inter-laboratories control and access results;
- possibility to connect the equipment to a scanner to import and monitor images taken at immunofixation and results for specific proteins;
- expanding the range of investigated parameters through the possibility to determine transferrin sialoforms (Fig.1) and normal hemoglobins (Hb F and A) and pathological ones (Hb S, C, D, E, Bart) in the new born baby, with excellent resolution;
- direct analysis of erythrocytes not washed, centrifuged or pelleted;
- elimination of routine interferences such as hemolysis, lactescent and jaundice sera and artifacts related to point where the sample was applied and presence of monoclonal compounds at low concentrations;
- low cost per analysis

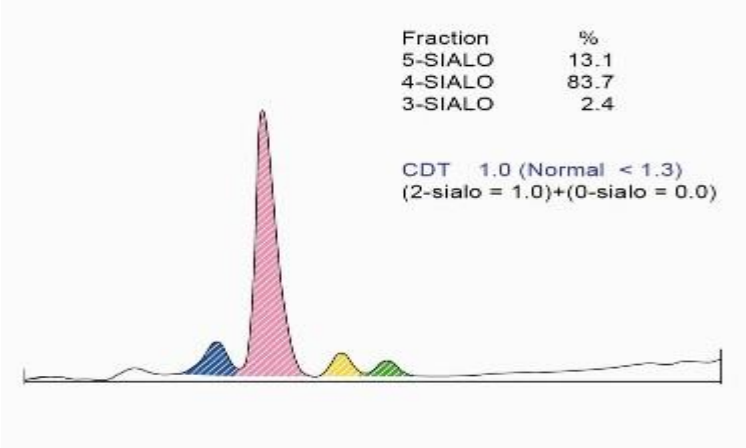

Fig. 1 Electrophoretic separation of transferrin sialoforms in the Capillarys system

QUALITATIVE DIFFERENCES BETWEEN CE AND AGE ELECTROPHOREGRAMS

For certain, electrophoresis of serum proteins has been the start off for biochemical investigations in any area of pathology, especially in view of monoclonal components' and acute phase proteins identification: alpha 1 anti-trypsin, alpha1 glycoprotein, haptoglobin, fibrinogen [2].

Any electrophoregram which raises suspicion about a monoclonal component should be followed by immunopheno-typing of that component. As later mentioned immunophenotyping is an expensive and laborious analysis, it is necessary for the protein separation

technique (used as screening test) to be extremely specific and sensitive.
Studies carried out by Clark [3] in normal human sera pointed out differences between electrophoretic models resulted from the two methods conducted in normal sera. One difference regards fractions resulted (albumin, alpha1 globulins, beta globulins, gamma globulins) which appear in reverse order on the two electrophoregrams (Fig.2, Fig.3). The explanation was the electrode where sample was pipetted, cathode in the case of AGE and anode for CE. Some samples presented with supplemental bands in alpha and beta mobility zones with no confirmation for the bands as monoclonal after immunophenotyping [3].
For sera with well represented monoclonal components, this comparison between the two methods points out comparable results.

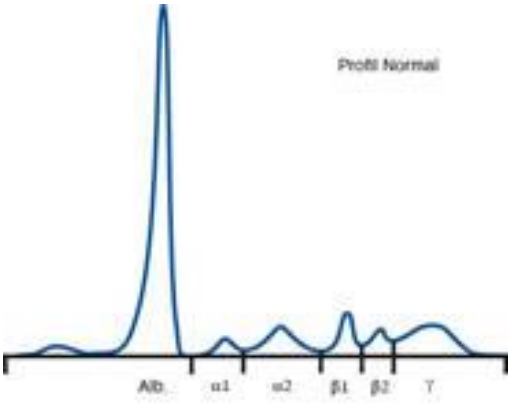

Fig.2 AGE electrophoregrams

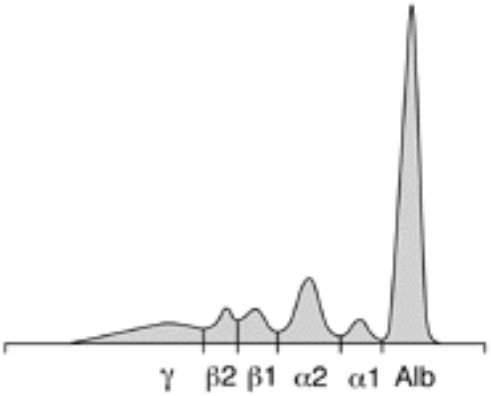

Fig.3 CE electrophoregrams

QUANTITATIVE DIFFERENCES BETWEEN CE AND AGE ELECTROPHOREGRAMS

As regards the quantitative aspect, a (strong or positive) correlation between CE and AGE was noticed for albumin, alpha2 and gamma globulins (r=0.99). For alpha1 globulins, results obtained using CE were at average, 2.2-fold higher than AGE [4,5]. These differences might be partially explained through the sialic acid and alpha1 increased contents which interfere with binding of proteins to the colored (staining) compound which is used in AGE. Considering artifacts the type of cryoglobulins or euglobulins, which have reduced mobilities and remain at the electrode where the sample is applied, CE proved clearly superior to AGE as price per analysis and time taken for immunofixation decreased. In addition, CE has the advantage of migration temperature under control through maintaining it at 35.5 and this fact reduces risk of cryoglobulins to precipitate during migration.
Assessment of monoclonal immuno-globulins could be revolutionized through utilization of CE with a micro HPLC component incorporated. CE will thus have a much higher resolution in comparison to AGE. The above specification for CE would confer high speed of separation, requirement for low-volume sample and a lower price (cost) per analysis [3].
CE does not raise this problem because in this technique, no colored (staining) compound is used. Another explanation would be absence of a base line of the Capillarys system software version. Results for beta globulins showed (weak) correlations on CE and AGE electrophoregrams due to differences of electrophoretic mobility of beta lipoproteins (between alpha2 and beta for CE, between beta type(s) for AGE. Differences among numbers of bands were reported as well for gamma globulins' zone and nevertheless were not confirmed

by immunofixation as monoclonal. These bands are due to proteins with post gamma mobility (C Reactive Protein- CRP and degradation products of C3). CRP at concentrations higher than 300 mg/l (which appear on electrophoregram as a weak band in the gamma globulins' zone) can interfere in determinations of gamma globulins. These values are rare and hence, frequency at which interference occurs is reduced.

By using the two methods results were comparable for paraproteins at high concentrations. CE proved to be more sensitive for monoclonal components at low concentrations (detection threshold 0.5 g/l).

Presentation of these comparative data (qualitative and quantitative) between the two methods supports choosing CE as viable alternative to classical electrophoresis. The main reason is the possibility for identification of weakly represented abnormal bands, which AGE misses because for CE reading values in relative percentages of fractions is performed at 214 nm without staining as compared to AGE. Use of staining (coloring) might induce artifacts as result of post-translational modifications of various proteins of samples to analyze. Also, staining time, concentration of staining compound and discoloration time, all can influence binding of staining compound to proteins and thus, quantification of separated fractions.

CONCLUSIONS

- Proteins' electrophoresis is a routine analysis, the agarose gel being the most used electrophoretic medium. Regardless automation of electrophoretic systems and availability of ready- to-use reagents, AGE is a relatively laborious technique exposed to multiple interferences.
- Capillary electrophoresis is a viable alternative to classical electrophoresis, especially because the most frequent interferences for electrophoretic techniques (hemolysis, jaundice and lactescent sera, as well as artifacts related to point of sample injection, presence of monoclonal components at low concentrations) have no effects on capillary electrophoresis.
- Electrophoretic separation of proteins from low-protein fluids (cerebrospinal fluid and urine) and also quantitative determination of glycosylated hemoglobin and transferrin's sialoforms using the multi-capillary system are important perspectives of development of electrophoretic techniques in the Capillarys system.
- Although the capillary electrophoresis is at present less available, it imposes itself as a more rapid, more sensitive method for the future than the agarose gel electrophoresis.

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CHRONIC PAIN IN OLDER ADULTS WITH DEPRESSIVE DISORDER

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Abstract. Depression and chronic pain are both highly prevalent conditions in older adults. Although very frequent, depression is largely underdiagnosed and undertreated amongst seniors. The main objective of this case control study is to investigate the clinical relationship between depressive disorder and chronic pain in a sample of 65 years of age and older inpatients. A total number of 174 participants living independently in their communities and without neurocognitive severe disorders were included, of which 87 with depressive disorder and an equal number of matched for age and sex controls. The rate of chronic pain was significantly higher in patients with depressive disorder compared to controls (p=0.008). There was a statistically significant positive correlation between the presence of chronic pain and age in controls ($\tau = 0.279$, $p = 0.002$) but not in patients with depression ($\tau = 0.146$, $p = 0.107$). Compared to men, women were more likely to have chronic pain when they also had depressive disorder ($\tau = 0.248$, $p = 0.021$). We report a high prevalence of chronic pain in elderly patients (56.89%) where musculoskeletal and neuropathic were the most frequent types. Older adults with depression and especially women are more likely to suffer from chronic pain.
Key words: elderly, depression, pain

DUREREA CRONICĂ LA PACIENŢII VÂRSTNICI CU SINDROM DEPRESIV

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Rezumat. Depresia şi durerea cronică sunt afecţiuni foarte frecvente în rândul vârstnicilor. Deşi are o prevalenţă mare, sindromul depresiv rămane adesea nediagnosticat şi netratat. Principalul obiectiv al acestui studiu caz-martor este de a investiga relaţia clinică dintre depresie şi durerea cronică într-un eşantion de pacienţi cu vârste de 65 de ani şi peste. În studiu au fost incluşi 174 de vârstnici independenţi funcţional şi fără tulburare neurocognitivă severă, dintre care 87 cu sindrom depresiv şi un număr egal de pacienţi cu vârste şi sex similare, în grupul martor. Prezenţa durerii cronice a fost semnificativ mai importantă la pacienţii cu depresie comparativ cu lotul martor (p=0.008). A fost identificată o corelaţie pozitivă şi semnificativă statistic între prezenţa durerii cronice şi vârstă în grupul martor ($\tau = 0.279$, $p = 0.002$) însă această corelaţie nu a fost semnificativă în grupul de pacienţi cu depresie ($\tau = 0.146$, $p = 0.107$). Este mai probabil ca femeile cu sindrom depresiv să aibă durere cronică comparativ cu bărbaţii ($\tau = 0.248$, $p = 0.021$). În acest studiu prevalenţa durerii cronice la vârstnici a fost mare (56.89%), cele mai frecvente tipuri de durere având origine musculoscheletală sau neuropatică. Prezenţa sindromului depresiv la vârstnici şi în special la femei creşte probabilitatea ca aceştia să sufere de durere cronică.
Cuvinte cheie: vârstnici, depresie, durere

INTRODUCTION

The world's population is aging rapidly. Epidemiological studies report that by the year 2050, almost a quarter of the population will be 60 years of age and older [1]. Among the multiple chronic

diseases highly prevalent in this age group, mental or neurological disorders account for 6.6% of all disability (disability adjusted life years-DALYs) and for 17.4% of Years Lived with Disability (YLDs) [2]. Major depression disorder affects approximately 7% of older people globally, anxiety disorders 3.8% of the world's older population and around a quarter of deaths from self-harm are among people aged 60 and over [3]. Clinically significant depressive symptoms are present in approximately 15% of community-dwelling older adults, in substantially higher proportions in medical inpatients and residents of long term care facilities and markedly increased rates in outpatients with chronic medical conditions [4-6]. Depression is largely underdiagnosed and undertreated amongst seniors and several reasons contribute to this fact such as measurement confounding in patients with disabilities or cancer, geriatric specific presentations or different presentations in the context of neurological syndromes as well as older patients' reluctance to report symptoms and accept treatment [6,7]. Especially in elderly persons, depression can cause loss of interest in living, hopelessness about the future and atypically somatic symptoms such as fatigue or agitation [8,9].

Current evidence suggests that older people experience pain and chronic pain more than any other segment of the population [10-12]. Recently there is increasing interest in the link between chronic pain and modifications in the nervous system in elderly and it is believed that the common pathogenic factor of chronic pain and depression would be neuroinflammation [13]. Elucidating the clinical relationship between depression and chronic pain bares the significant importance of interdisciplinary management of senior patients when these two conditions are comorbid and highlight the challenges associated with diagnosis, treatment and monitoring [13,14]. Studies conducted in the general population have shown that patients diagnosed with major depression disorder are three times more likely to suffer from non-neuropathic pain and six times more likely to suffer from neuropathic pain [15]. Conversely, chronic pain increases the risk for depression between 2.5 and 4.1 times [16,17]. However, there are very few studies on the etiology and specific subtypes of chronic pain and its association with depression in the elderly population.

METHODS

This is a case control study that investigates the association between depression and chronic pain in elderly patients. The objectives of this study are to evaluate the prevalence of chronic pain and different subtypes of chronic pain as well as to assess the relationship between depressive symptoms and reported chronic pain among older patients with regard to gender and age.

All study participants were inpatients admitted to the National Institute of Gerontology and Geriatrics "Ana Aslan", Bucharest, on referral from their GP or other specialists for various subacute or chronic conditions during October 2015 - July 2016. The study group comprised of patients diagnosed with depressive disorder at least 3 months prior to recruitment and 65 years of age and older. The control group included patients matched for age (±1 year) and gender and without depressive symptoms in their medical history and/or a Geriatric Depression Scale-15 items score of ≤4 at admittance [18,19]. For the present study patients with severe neurocognitive disorder were excluded.

The data were collected from patients' medical records and the presence and type of chronic pain were documented by interviewing each study participant. Chronic pain is considered a condition in itself and although the definition varies among specialists, common criteria are persistent pain for at least 3 months or beyond the duration of its cause [20].

According to the International Classification of Diseases, Eleventh Revision, pain syndromes can be clinically classified into seven groups based on the underlying etiology: chronic cancer pain, chronic neuropathic pain, chronic musculoskeletal pain, chronic post-traumatic or postsurgical pain, chronic visceral pain, chronic headache and orofacial pain and chronic primary pain of unidentifiable causes [20].

The frequency distribution was used to identify the prevalence of chronic pain and its subtypes among study participants. The presence of chronic pain among patients with and without depressive disorder was assessed with the McNemar's test. To evaluate the frequencies of chronic pain in different age and gender groups we used the Kendall rank correlation analysis. We used a 95% confidence interval (CI) and a value of $p<0.05$ for statistical significance. Statistical analysis was performed with DATAPLOT programme.

RESULTS

After checking against the eligibility criteria, a total number of 174 patients were included, the study and control groups comprising of an equal number of 87 patients each. The mean age in the study sample was 75.18 years and the majority were women (Tab. I). Most patients were living in urban areas, had either high school or university level education and an income above national average pension. Compared to controls, more patients diagnosed with depressive disorder were living in urban areas, had lower incomes and university education, although the numbers were comparable between groups (Tab. I).

Tab. I Sample demographic and socio-cultural characteristics.

Characteristic	Cases (N=87) Mean (SD)/%	Controls (N=87) Mean (SD)/%	Sample (N=174) Mean (SD)/%
Age	75.17 (5.45)	75.2 (5.7)	75.18 (5.56)
Female	77.01		
Living in rural area	33.33	42.52	37.93
4-8 years of formal education	32.18	36.78	34.49
9-12 years of formal education	36.78	39.08	37.93
>12 years of formal education	31.03	21.83	27.58
Low income*	44.82	40.22	42.52

*Medium pension/month expressed in local currency RON [National Institute of Statistics. Press Release No. 66 March. 2016. Number of pensioners and medium monthly pension in forth trimester 2015. http://www.insse.ro/cms/files/statistici/comunicate/com_trim/nr_pensionari/a15/pensii_tr4r15.pdf;
National Institute of Statistics. Press Release No. 72 March. 2017. Number of pensioners and medium monthly pension in 2016. http://www.insse.ro/cms/sites/default/files/com_presa/com_pdf/pensii_2016r.pdf

The prevalence of chronic pain in both study and control groups was high (68.96%, respectively 44.82%) (Tab. II) and statistically significantly higher among patients with depressive disorder compared to controls ($p=0.008$) (Tab. III). The most frequent type of chronic pain in both groups was of musculoskeletal origin (78.33% in cases with chronic pain respectively 58.97% in controls with chronic pain) followed by neuropathic and visceral etiology. There were no cases of cancer or orofacial chronic pain. Only four patients in the study group reported chronic pain related to humerus, distal radius fracture and postcholecystectomy and for two others there was no objectively identifiable cause for their recounted chronic pain. Two other patients in control group had chronic pain related to a previous traumatic injury (Tab. II). The majority (68.33% in cases respectively 61.53% in controls) had more than one chronic pain condition. Given the sample size limitation we could not investigate the influence of depressive disorder on each different subtype of chronic pain.

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Tab. II Prevalence of chronic pain and its' sub-types

Chronic pain and its' Sub-Types	Cases (N=87) %	Controls (N=87) %
chronic pain	68.96	44.82
neuropathic	38.33	33.33
musculoskeletal	78.33	58.97
post-traumatic or postsurgical	6.66	5.12
visceral	35	23.07
primary	2.29	-

Tab. III. Chronic pain in study and control groups

McNemar's Test

Cases n=87	Controls n=87		p value
	no	yes	
no	9	18	**0.008**
yes	39	21	

The majority of patients in our study sample were 71-80 years old, around 1 in 5 was 65-70 years old and 1 in 7 was over 80 years of age. The prevalence of chronic pain increased with advancing age in both study and control groups and it was very high in the oldest old age segment (73.33% respectively 64.7%). There was a statistically significant positive correlation between the presence of chronic pain and age in controls ($\tau = 0.279$, $p = 0.002$). In patients with depressive disorder this association was not statistically significant ($p>0.05$) (Tab. IV).

- Compared to controls, a very high proportion of women with depressive disorder also suffered from chronic pain (73.13% respectively 46.26%). Depression did not seem to influence the rate of chronic pain in men (55% of males in the study group and 50% of males in the control group). There was a statistically significant correlation between chronic pain and gender in patients with depressive disorder and even though chronic pain was more prevalent in women than in men in controls, this aspect was not significant (Tab. IV).

Tab. IV Relationship between age, gender and chronic pain

Chronic pain %	Age (years)				Kendall tau correlation	Gender		Kendall tau correlation
	65-70	71-75	76-80	>80		F	M	
cases	63.15	68	71.42	73.33	$\tau = 0.146$, $p = 0.107$	73.13	55	**$\tau = 0.248$ $p = 0.021$**
controls	33.33	40	45.83	64.7	**$\tau = 0.279$, $p = 0.002$**	46.26	40	$\tau = 0.005$ $p = 0.962$

numbers in bold represent statistical significance

DISCUSSION

The analysis of our study sample showed a high prevalence of chronic pain among older adults. More than one in two patients admitted in tertiary geriatric care for various chronic and subacute conditions reported chronic pain. The majority of chronic pain cases were of multiple etiology and the most frequent type was of musculoskeletal origin followed by neuropathic and visceral pain. Our results are consistent with others reported in literature considering that our sample was selected from inpatients admitted for subacute or chronic conditions. In one community dwelling population based study the rate of chronic pain was 38.94%, of them 57.71% had more than one type of chronic pain and musculoskeletal pain was the most common [21]. Another survey

that took place in Poland reported that chronic pain affected 42% of respondents aged 65 years and over (48.6% of women and 35.8% of men) [22]. A similar population survey in Spain described that the frequency of pain increased with age, reaching 42.6% in people older than 65 years and the most frequent type of pain was musculoskeletal [23]. In older Swedish adults the prevalence of chronic pain was found to be 38.5% and more common among females and among adults over 85 years of age [24]. In a sample of nursing home residents in Italy with a mean age of 82.2+/-9 years, the rate of chronic pain was as high as 82.9% [25].

In our study, we found that the prevalence of chronic pain was significantly higher in patients with depressive disorder. Another general population study reported that patients suffering from a major depressive disorder are three times more likely to suffer from non-neuropathic pain and six times more likely to suffer from neuropathic pain [26]. It has been shown that 13% of the elderly suffer from both depression and chronic pain and depressive symptoms contributed significantly to the prediction of impairment associated with pain [27]. The rate of chronic pain significantly increased with age in controls as well as in patients with depressive disorder but in the latter this association was not significant. These two findings signify that in the oldest old depression is not necessarily associated with chronic pain while at younger ages, patients with depression are more likely to suffer from chronic pain. There was a significant correlation between gender and the presence of chronic pain in our study group, women with depressive disorder being more likely than men to have chronic pain. Similar results were published by an observational cohort study that reported older women being more likely to suffer from chronic pain if they also have depressive disorder [28]. No large studies have been conducted on the relationship between different subtypes of chronic pain and depression in the elderly. The main limitation of our study was the sample size and future prospective studies are still needed to elucidate how depression influences different pain conditions in older adults.

The significant association between depression and chronic pain in the elderly found in our study is even more important in the light of the findings of a recent large study. This particular population-based and families of twins study reported an increased co-occurrence of chronic pain, depression and cardiovascular disease in two independent cohorts suggesting a shared genetic contribution [29].

CONCLUSION

Chronic pain is highly prevalent in older age and its rate increases with age. Musculoskeletal and neuropathic pain syndromes are the most frequent type of pain in seniors. The presence of chronic pain is significant among older adults with depression while this association seems to be less important in the oldest old. It is therefore necessary to identify and manage depressive disorders in elderly because these patients are more likely to seek medical care for chronic pain. Especially in older women with depression chronic pain is very common.

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ASPECTS OF STRESS AS A RISK FACTOR IN CARDIOVASCULAR DISEASES - STUDY PERFORMED ON A GROUP OF PATIENTS FROM NIGG AND COLŢEA HOSPITAL

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Abstract. Our work studies the relationship between stress and cardiovascular diseases (CVD) on 93 elderly inpatients. Some biologic and psycho-social stressful aspects are analyzed within a study lot with cardiovascular pathology (60 patients from NIGG and Colţea Hospital) vs. the control lot (33 patients) who has also chronic pathology, but fewer and less serious CVD conditions. The tests assess: the subjects' social situation, different stressors in elderly life (Miller questionnaire), global stress (Well-Being Scale) and depression (Geriatric Depression Scale, short version). The descriptive analysis of the data reveals in the study lot, compared to the control lot: – antecedents of higher workplace stress and – stress of poverty (low pensions, fewer than 350 lei, in 12.3% subjects). The order of stressors in elderly study lot is: CVD (63.5%), fear of falling (61.22%), fear of pain (57.7%), fear of dependence in care (56.8%), loneliness. In the control group the high weights are caused by: fear of pain (66.67%), medicines costs (51.52%) and loneliness (45.45%). Global stress is lower in the control group compared to the study sample: while good and satisfactory psychological state is assessed for 67.6% patients from the healthy sample, the same evaluation is found only in 27.3% patients from the cardiovascular patient's sample. Our study supports the idea of multifactoriality in CVD determination by presenting the interdependence between stress and the three dimensions of health: (a.) biological component (cardiovascular disease/generated disability); (b.) social component (dependence, isolation) and (c.) psychological component (loneliness, uselessness).

Key words: stress, cardiovascular pathology, three-dimensional assessment of health

ASPECTE ALE STRESULUI CA FACTOR DE RISC ÎN BOLILE CARDIOVASCULARE - STUDIU REALIZAT PE UN LOT DE PACIENŢI DIN INGG ŞI SPITALUL COLŢEA

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Rezumat. Lucrarea studiază relaţia dintre stres şi bolile cardiovasculare (BCV) pe un lot de 93 pacienţi vârstnici. S-au analizat câteva aspecte bio-psiho-sociale considerate stresante într-un lot de studiu (60 pacienţi din INGG şi spitalul Colţea) cu afecţiuni cardiovasculare vs. lotul martor (33 pacienţi) cu polipatologie cronică, dar BCV cu pondere şi gravitate reduse. Testele utilizate evidenţiază: situaţia socială, tipurile de stres din viaţa vârstnicilor (T.W.Miller), stresul global (Well-Being Scale) şi depresia (Geriatric Depression Scale, versiunea scurtă). Analiza descriptivă a datelor relevă în lotul de studiu, comparativ cu lotul martor: -antecedente de stres psihic şi fizic mai mare la locul de muncă; -stresul sărăciei (pensii sub 350 lei la 12.3%). Ordonarea aspectelor stresante în lotul de studiu, situează pe primele locuri: BCV (63.5%), teama de căderi (61.22%), teama de dureri (57.7%), dependenţă în îngrijire (56.8%) şi singurătatea. În lotul de control, cele mai mari ponderi le au stresul

provocat de: teama de dureri (66.67%), costul medicamentelor (51.52%) şi singurătatea (45.45%). Stresul global este mult scăzut în lotul martor comparativ cu lotul de studiu (stările psihice: bună + satisfăcătoare ajung la 67.6% la sănătoşi şi numai la 27.3% la bolnavii cardiovasculari). Studiul susţine ideea de multifactorialitate în determinarea BCV prin prezentarea interdependenţei dintre stres şi cele 3 dimensiuni ale sănătăţii: (a.) componenta biologică– boala cardiacă/incapacitatea generată; (b.) componenta socială- dependenţa socială, izolarea şi (c.) componenta psihologică (singurătatea, inutilitatea).
Cuvinte cheie: stres, patologie cardiovasculară, evaluare tridimensională a sănătăţii

INTRODUCTION

The stress is the adaptation response of the organism to the environment. The significance of perceived discomfort can have positive effects by mobilizing personal resources or, on the contrary, can be perceived as negative. In this case it can affect the body, thoughts and behavior. When the distress is intense, over a long period of time, it can be difficult to manage, consuming the individual's energy; the feeling of exhaustion appears and aggravate health problems. The European Charter on Cardiovascular Health (Article 3) insists on the idea of multifactoriality in the determination of cardiovascular diseases (CVD) and on addressing the therapy of these factors both individually and socially. Excessive stress can be a very important factor in these diseases. Literature abounds in studies on stress and the multitude of relationships with the disease [1].

The first description of the relationship between stress and illness belongs to W. Osler (in 1910), who noted that angina pectoris is a disease commonly affecting the business people [2].

An article in the Journal of the American College of Cardiology recalls an essential fact: the heart has the most to suffer, as stress creates a whole environment in which heart attack or sudden death become more likely [3].

Researchers in University College London (UCL) show that workplace stress is a risk for symptoms such as hypertension, increased levels of cholesterol and serum glucose and overweight /obesity. Hormones, which endocrine glands release into the bloodstream when stress occurs, have also the function of mobilizing cholesterol and other fat deposits to provide muscles with the energy they need for a special need. When the expected shock does not occur, however, cholesterol and other unused fats adhere to the walls of the arteries, where they remain stored. In this way, atherosclerosis is favored [4,5].

MATERIALS AND METHODS

Our work studies the relationship stress-CVD on 93 elderly inpatients. The study group, consists of 60 subjects with cardiovascular disease (18 males and 42 females), patients from NIGG and from Colţea Hospital. The control group has 33 subjects (7 males and 26 women) with chronic polypathology (osteoarticular and digestive diseases have higher weights, and CVD are much reduced; in general, the selection of subjects with coronary diseases has been avoided). Average ages are close: 67.57 years in the study lot and 64.67 in the control group.

The selected tests assess:

-Stress by a complex stress test represented by the General Well-Being Scale (GWBS) [6];

-The stresses in elderly life (Questionnaire after T.W. Miller) [7];

-Social status;

-Depression by Geriatric Depression Scale (GDS) Yesavage et al., 1983 - short version [8];

Chronic pathology data are collected from the NIGG clinics, but also from Medical Section of Colţea Hospital.

RESULTS AND DISCUSSIONS

(I) Chronic polypathology

Pathological load across the whole sample was high, of ***7.1 diseases*** *per subject*.

The Fig. 1 shows in the *control* group an excess of diseases, namely: rheumatic, digestive, respiratory diseases and neurotic syndrome, compared to the ***study*** group. In the ***study*** group compared to the *control* group, positive percent differences are found in: hypertension (25%), ischemic cardiopathy (50%), diabetes mellitus (10%), obesity (17.7%) and neurological diseases (10%).

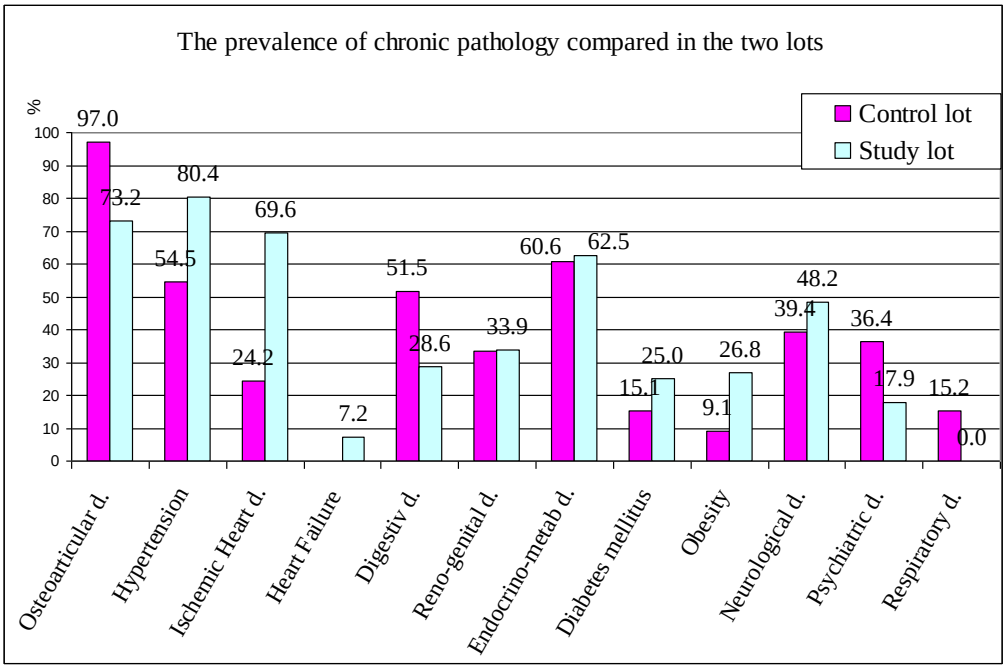

Fig. 1 The percent of chronic pathology in the two lots

(II) Types of psychosocial stresses present in the groups

(1) Personal antecedents of stress

Tab. I Occupational stress during active period

Type of stress	Study group (%)	Control group (%)
Psychological stress	**63.2**	54.55
Physical stress (intense physical effort)	**40.4**	24.24
Working in a toxic environment (also a physical stress)	38.6	39.39

(2) Income size stress

Income may be another type of stress present at all ages. The income of the analyzed subjects has an average of 951.18 lei and a standard deviation of 742.20 lei (a non-homogeneous lot from this point of view).

Tab. II Income size of the subjects in the two groups

Pensions	Study group (%)	Control group (%)
0 – 349 lei	**12.3**	3.0 (ns)
350 – 999 lei	54.4	54.5
1000 – 4400 lei	33.3	42.4

Often the income depends on the educational level. Tab. III illustrates a slightly weaker school education for CV patients: 17.7% of them have primary school, and 9% less have graduated from high school than those in the control group.

Tab. III The educational level

	Study group (%)	Control group (%)
Primary school (2-4 classes)	**17.7**	ns
Gymnasium level	36	36.4
High school	46.3	**54.6**

(3) Marital status and self-evaluation of social relationships

- In Tab. IV, although there are fewer widowers and alone ones in the study group than in the control group, due to the more serious pathology there is a tendency to isolation: they recognize in 25.5% cases that they have reduced their social relationships (5 times more than in the witness subjects) and claim they feel disadvantaged by illness or age. This situation is due in part to the depressed state of some of them. Instead, 69.7% of the healthiest in the control group declare they are satisfied with their social network and in double proportion to the more sick (63% and 32% respectively) say they can still make new acquaintances.

Tab. IV Marital status and some aspects of self-evaluation of social relationships

	Study group (%)	Control group (%)
Widower	28	33.3
Living alone	34.1	42
Pleased of their social relationships	57	**69.7**
Feeling alone, disadvantaged by illness or/and age	7	0
Have restrained social relations a lot	**25.5**	5
Ability to make new acquaintances	32	**63**

(4) The ordering of frequent stresses in elderly life by weighs, in the two groups

Miller's questionnaire enumerates numerous stresses, both existential and everyday life ones. In the study group, they are more related to the serious pathology CVD and the disability generated by it. In the witness lot, existential stresses are higher.

Anyway, we see that the study group considers the CVD stress as the most prominent (it occurs in 63.5% of cases); the control group considers the chronic pains generated by their pathology as the highest stressor (66.7%).

Cardiovascular diseases, as they get worse, may generate disabilities. Having certain perceptions, those patients are afraid of following (Tab. V):

- Falling (3 times more than the healthier patients);
- Dependence in personal care and dependence in housekeeping (almost 2 times more than the control group);

- Traveling outside the house (a stress 3 times higher than that of those healthier) and
- Using the public transport (it is also 3 times higher than the percent from control group);
- Hospital admission alarms 8% more those in the study group;
- The multiple problems caused by illness/incapacity and hence, the multitude of medical assistance problems represent a very high stress -a seven times (!) higher stress in cardiovascular patients compared to the healthier group.

- All of these events represent **daily stresses**, particularly annoying for our sick patients.

Tab. V The more frequent stresses in the study group

STRESSES	Percentage in study group %	Percentage in control group %
Average for all stress groupings	40.3	23.8
1. Stress of cardiovascular diseases	63.51	30.30
2. Fear of fallings	61.22	21.21
3. Dependence in house keeping	59.18	36.36
4. **Medicines costs**	**58.14**	**51.52**
5. Dependence in activity daily life	57.14	36.36
6. Traveling out of the house	38.78	12.50
7. **Uselessness**	36.73	30.30
8. **Unexpected death**	32.65	21.21
9. Hearing problems	30.61	21.21
10. Public transport	26.53	9.09
11. Medical assistance problems	22.45	3.03
12. Hospital admission	20.41	12.12

Everyday stresses are also related to costs (Tab. V, VI and VII):

- *The high price of medicines* - Those with a rich pathology, especially CVD, are particularly concerned about the cost of the medicines they need continuously. They feel they strongly depend on them, representing their chance for being alive and well being. Thus, this stress appears in 58.14% respondents, compared to those in the control group where they are 51.52%.
- The *costs of utilities* are perceived more by the healthier (with more than 10 percent extra) compared to the cardiovascular subjects.
- *Food costs* are a cause of equal concern for both groups.

Finally, in some circumstances, 16.33% patients from the study lot feel threatened by admission to a nursing home, a stress that the control group does not have at all.

Among the **existential stresses** we mention, with moderate weights: the feeling of uselessness and the fear of unexpected death- the latter appearing at a frequency of 11.5% higher in the study group, than at the healthy subjects (Tab. V).

Higher stresses in subjects from the control group are only six (Tab. VI):

- the stress of pain, at the highest share of all the stresses of the whole lot (66.67%);
- high utilities costs stresses;
- certain **existential stresses**:
  - fear of staying alone, without relatives;
  - fear of staying alone, without friends;
  - fear of death.

Tab. VI The stresses more frequent in the control group

	Percentage in study group %	Percentage in control group %
Average for all stress groupings	40.3	23.8
1.Pain stress	59.18	66.67
2. Cost stress for **household utilities**	34.69	45.45
3. Fear of **losing close relatives**	32.65	42.42
4. Fear of **death**	24.49	30.30
5. Stress of **losing friends**	14.29	30.30
6. The stress of **caring for a sick person**	14.29	18.18

In the Tab. VII., the assessment of the frequent stresses reveals the psychosocial stress of loneliness on the first places: 45.45% of the witnesses (3rd place in the "stress scale") and 42.86% of the cardiovascular group (4th place). Concerning the stress of losing the close ones, it is more frequently expressed by those in the witness group (42.42%) compared to the study group (32.65%). We can assume that such existential stresses are less painful for some CVD patients, who are somehow are resigned to the fate. (We also saw in the study group that fear of death is lower with 6 percents, comparative the control group).

Tab. VII Stressors with the same frequencies in both groups

	Percentage in study group (%)	Percentage in control group (%)
Average for all stress groupings	40.3	23.8
1. **Loneliness**	42.86	45.45
2. Stress for eye problems	40.82	39.39
3. The cost of **food**	40.82	39.39
4. Stress of memory loss	36.73	36.36
5. Fear of **remaining alone** after the relatives' death	34.69	36.36

(5) Global stress evaluation by the General Well-Being Scale (GWB)

Our patients also have been evaluated for global stress by The General Well-Being Scale (GWB) which focuses on one's subjective feelings of distress or psychological well-being. The scale includes both negative and positive questions and it assesses how the individual feels about personal state. Its items cover six dimensions: anxiety/strain or relaxation; depression or cheerfulness/ optimism; degree of (self) control of emotional states; interest in everyday life; energy, vitality level; care for one's own health. Considering only the percentages in which these characteristics were within the normal range, we obtained a comparative table:

Tab. VIII Positive aspects from General Well-Being assessed in our lots

	Study lot	Control lot
Control of emotional states	27.5	21.2
Relaxation (no anxiety)	30.2	30.3
Optimism (no depression)	37.2	**57.6**
Interest in everyday life	***26.8***	12.1
Energy (good level)	27.9	**48.5**
Concern for their own health	***29.3***	12.1

By comparing the two lots regarding **the components of this stress score**, we find differences in favor of the control group: the level of a good psychological state, with optimism, cheerfulness (57.6% vs. 37.2% in the study group) and a higher energy level (48.5% vs. 27.9%). But the concern for their own health and their interest in daily life are lower in the control group compared to the study group.

Tab. IX shows an overall characterization of the stress level of the subjects investigated in the two groups. In the study group, good or satisfactory psychic status is present only in 27.3% subjects, while in the control group in 66.67% cases. The negative stress appears in 28.7% people in the study group and in 30.3% subjects in the control group. The stress area has a significant percentage (26%) in the study group and it is non-significant in control group.

Tab. IX The evaluation of total stress score

	Study group (%)	Control group (%)
Good psychological state	12.6	21.21
Satisfactory condition	14.7	45.45
Stress zone	25.9	3.03 (ns)
Distress zone	19.6	21,21
Significant distress	7.7	6.06
Severe distress	1.4	3.03 (ns)

In the control group, the general well-being is 21.21%, and 45.45% claims to have a satisfactory psychological state. In contrast, in the study group most (25.9%) feel their stress on the verge of becoming an issue.

The multiple stresses of elderly life can lead to depressive states of varying intensity, being linked with chronic ubiquitous pathology. Assessed by Geriatric Depression Scale, those evaluated as normal, without depression, appear in 48% elderly with CVD and in 57.6% healthier subjects.

In the control group there are 10% more those with low scores in the symptom-atology of depression. With 6% more in the study group, there are higher values for the depression test with mild and moderate depression. And just 3% more in the control group have a status of equivalent severe depression (12.12% in control group and 9.6% in study group).

In Tab. X we analyze the quality of sleep and its influence on the level of energy, interest in life, the tendency to be optimistic /cheerful to the state of relaxation and emotional control. Stress (or well-being) correlates significantly with the sleep of the patients.

A restful sleep means a good level of energy, a relaxed mood and a good emotional control. We might say that the sleep is a true therapy to reach a good-feeling level and to be mentally balanced.

Tab. X Correlations of well-being components with sleep and its quality

Components aspects of global stress Score (GWB)	Peaceful sleep		Hours of sleep	
	r=..	p=…	r=..	p=…
Good level of energy	.**409**	.000	**.341**	.000
Relaxed mood	**.329**	.000	**.290**	.002
Emotional control	.293	.000	.201	.030
Interest in life	.273	.000		
The tendency to joy and optimism	.258	.005	.272	.003
Concern for their own health	.231	.003	.280	.002

CONCLUSIONS

The study supports the idea of multifactoriality in CVD determination by presenting the interdependence between stress and the three dimensions of health: biological component (cardiovascular disease/generated disability); social component (dependence, isolation) and psychological component (loneliness, uselessness).

The global stress in the study lot is higher than in the control lot, if we compare their states of well-being: only 27.3% for the CVD subjects and 66.67% for the healthier patients.

All the patients are affected by various stresses, with various weights, both everyday stresses and existential ones.

Regarding the link stress-biological component of health, we underline the high CVD prevalence in the study group compared to the control group: hypertension is higher by 25%, ischemic cardiopathy by 50% and heart failure exists only in the study group. So, statistically, subjects of the study group put the CVD stress on first place in their stresses ordering (it occurs in 63.5% cases); the control group considers the chronic pains on the first place (in 66.7% subjects). Due to the physical disability, a consequence of the serious diseases, the CV patients experience fear of: falling, traveling outside their home and fear of using the public transport. Also, the functionality of social role (in domestic activities and the support of their families) is more affected by their pathology. Dependence in everyday activity represents another social stress component (it reaches 57.7% in the study lot, two times higher than in the control lot). And finally, another frequent social stress is represented by high costs (for medicines, household utilities and food) and low pensions.

Such stressful social problems can generate sometimes feelings of: depression, uselessness, fear of loneliness and fear of death. All represent the psychological component of health, linked to stress.

Concluding, it can be said that the treatment of CVD in elderly must be approached globally, not just by drug therapy. Ideally, it would be advisable to alleviate the sources of stress and depression: physical sources, socio-economical and psychological ones. For the latter, some prominent method can be mentioned: psychological therapy, counseling and support groups, where the patients can socialize or ask for help.

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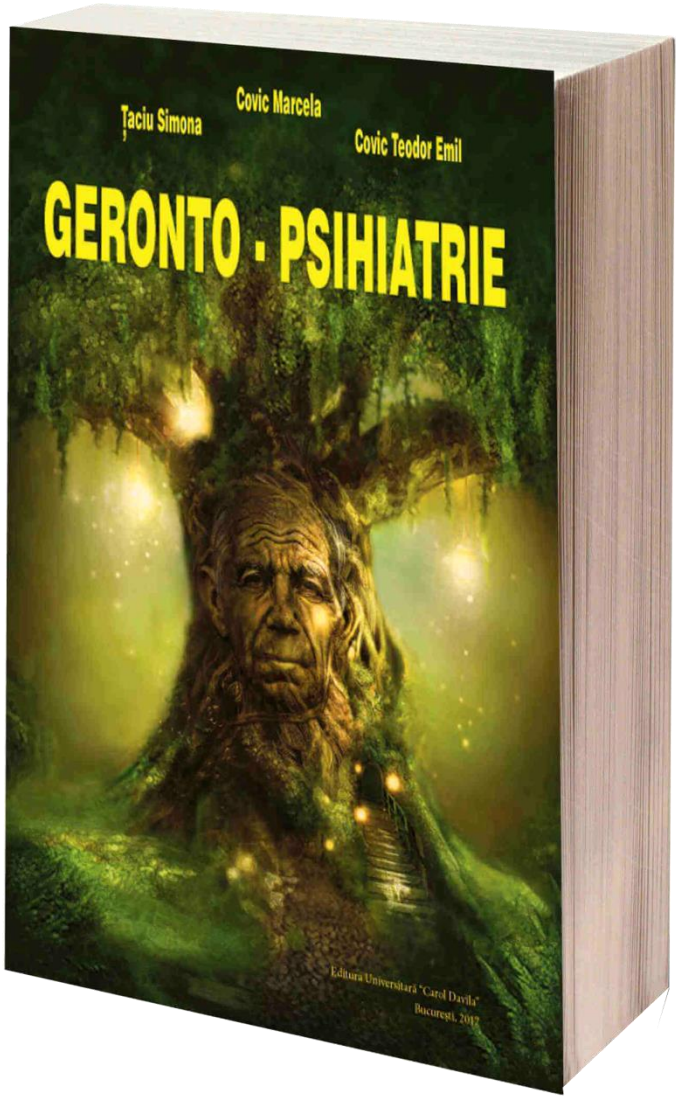
BOOK PRESENTATION
"Geronto-Psihiatrie" ("Geronto-Psychiatry")
by Covic Marcela, Țaciu Simona, Covic Teodor Emil
Editura Universitară "Carol Davila", Bucharest, 2017, 622 pages



"Geronto-psihiatrie" - "Geronto-psychiatry" written by Marcela Covic, MD, is the outcome of a lifelong experience in treating older patients, created over several years. It is the result of an original act offering a unique perspective: that of a psychiatrist who became also a geriatrician, with a deep involvement in both medical specialties.

Even from the beginning one could easily notice its systematic and well-organized structure. For a better understanding of the differences between normal and pathologic the author started with a broad review of data regarding the process of brain aging described in the general context of aging and various theories that form the basis for explaining the main characteristics of older people. The monograph continues with description of the mechanisms underlying the process of neurogenesis, neuronal proliferation and formation of the central nervous system, connected to neuronal migration, synaptogenesis, remodeling, neuroplasticity and apoptosis. They are followed over the whole period of human development from intrauterine life to adulthood and old age. Process of brain aging, considered as a normal aspect seen in older people, is described in its various aspects: morphologic, vascular, biochemical, metabolic, regarding neurotransmitters. There are several subchapters with many practical examples concerning prevention of brain aging, factors favoring a "successful aging" and risk factors for brain aging.

Often the characteristics of psychiatric disorders are less well known to young medical graduates because of their complexity. Consequently the chapter regarding psychiatric diseases is very useful as a solid background in this field. Corroborating characteristics of psychiatric diseases with their classification together with highlighting the specific patterns of psychiatric disorders in older people make a clear introductory picture mandatory for a better understanding of this spectrum of diseases beyond the age of 65 years. An essential chapter is

the psychiatric examination that combines theoretical aspects with an exceptional practical experience of Dr. Marcela Covic in the field of old age psychiatry.

An important chapter is that regarding semiology of psychic functions. It contains a systematic review of attention, perception, memory, thinking, graphic and verbal expression, affectivity, will, motor activity, instinctive manifestations, consciousness and personality, featuring the characteristics of older people. It continues with the main psychiatric syndromes that are encountered in old age, followed by main neurocognitive disorders seen in geriatric medicine.

Next there are two chapters very useful for the differential diagnosis of neurocognitive disorders: delirium and depression. Besides clinical picture and positive and differential diagnosis, the author presents various therapeutic options, possible drug interactions and an algorithm for the treatment of depression.

Older patients often report sleep disorders. The chapter on this topic is therefore very important for a geriatrician but also for any physician involved in dealing with patients beyond the age of 65 years. It describes aspects of normal sleep in older people together with a clear classification of sleep disorders and a positive and differential diagnosis of conditions generating sleep alterations in old age, followed by therapeutic interventions.

The last chapter of the monograph presents psychopharmacology in the older people. It describes specific patterns of pharmacokinetics and pharmacodynamics influenced by transformations that accompany the process of aging.

The appendices at the end of the monograph contain several scales of assessment that are very useful for daily activity of specialists involved in caring for older patients. They are dedicated to evaluation of cognitive function, mood and functionality.

"Geronto-psihiatrie" - "Geronto-psychiatry" by Marcela Covic, MD, demonstrates a vast experience in complex approach of older patients incorporating the perspective of an excellent psychiatrist with that of a very good geriatrician. Moreover, it adequately combines a special analytical mindset with an exceptional capacity of synthesis. All these qualities can be found in this monograph that one can read easily and with pleasure because of the clarity of the ideas presented. In addition it is a very useful tool for day to day medical activity of geriatricians, psychiatrists, but also other specialists that deal with the difficult task of taking care of older patients.

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SECȚIUNILE. Manuscrisele care prezintă rezultatele unor studii originale trebuie să conțină maxim 2500 de cuvinte și să fie organizate în următoarele secțiuni: Introducere, în care vor fi specificate clar obiectivele și ipotezele studiului; Materiale și Metode; Rezultate; Discuții; Concluzii. In secțiunea "Rezultate" vor fi incluse tabelele, graficile și figurile împreună cu titlurile și legendele lor.

BIBLIOGRAFIA. Bibliografia va cuprinde maxim 30 de titluri reprezentând articole publicate recent (în ultimii 10 ani). Se acceptă articole mai vechi dacă prezintă importanță deosebită în domeniul respectiv. Titlurile bibliografice se vor ordona în funcție de apariția în text. La fiecare lucrare vor fi menționați doar primii trei autori urmați de *et al.* Citarea articolelor se face după următorul model:

Pentru articole din revistele științifice: Shapiro A.M.J., Lakey J.R.T., Ryan E.A., et al. *Islet transplantation in seven patients with type 1 diabetes mellitus using a glucocorticoid-free immunosuppressive regimen*. N. Engl. J. Med., 2000, vol. 343, 4: 230-238.
Pentru articole în format electronic*:* Niki E. *Role of vitaminE as a lipid-soluble peroxyl radical scavenger: in vitro and in vivo evidence*, Free Radical Biology and Medicine, 2014, 66: 3–12. http://dx.doi.org/10.1016/j.freeradbiomed. 2013.03.02223557727.
Pentru capitol sau subcapitole din monografii sau tratate*:* Goadsby P. J. *Pathophysiology of headache*. In: S. D. Silberstein, R.B. Lipton and D. J. Dalessio (Eds.), Wolff's headache and other head pain, 7th ed. 2001, Oxford, England: Oxford University Press, pp. 57-72.
Pentru articole prezentate la conferințe*:* Brown S. & Caste V. *Integrated obstacle detection framework.* Paper presented at the IEEE Intelligent Vehicles Symposium, May 2004, Detroit, MI.
Pentru articole prezentate la conferințe care apar online: Balakrishnan R. *Why aren't we using 3d user interfaces, and will we ever?* Paper presented at the IEEE Symposium on 3D User Interfaces March 25-26, 2006. doi:10.1109/VR.2006.148

FIGURILE. Figurile vor fi realizate profesional. Titlul va fi scris sub figura, format Times New Roman 10, iar pentru numerotare se vor utiliza cifre arabe. Fișierele cu imagini trebuie să fie în format JPG sau TIF iar rezoluția trebuie să fie de 300 dpi.
Dacă sunt incluse imagini ale unor pacienți, este necesar consimțământul scris al pacientului pentru difuzare publică sau pacientul trebuie să fie neidentificabil.

TABELELE. Titlul fiecărui tabel va fi scris deasupra, iar pentru numerotare se vor folosi cifre romane, format Times New Roman 10. Notele explicative vor fi în partea de jos a tabelului. Nu se accepta repetarea rezultatelor din tabel prin grafice.

EXPRIMAREA MULȚUMIRILOR. Vor fi menționate înaintea bibliografiei, utilizand maximum 30 cuvinte. Se pot exprima mulțumiri pentru sprijinul acordat în desfășurarea proiectelor de cercetare.

ABREVIERILE. La prima utilizare in text, abrevierea (acronimul) trebuie sa fie precedat de expresia integrală.

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UNITĂȚILE DE MĂSURĂ. Inălțimea, greutatea, volumul, lungimea vor fi exprimate în unități de măsură din sistemul internațional (centimetru, kilogram, litru, unități decimale ale litrului, metrului). Temperaturile vor fi specificate în grade Celsius. Presiunea arterială va fi precizată în mmHg. Rezultatele analizelor laboratorului clinic vor fi exprimate în unitățile de măsură din sistemul internațional SIU.

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