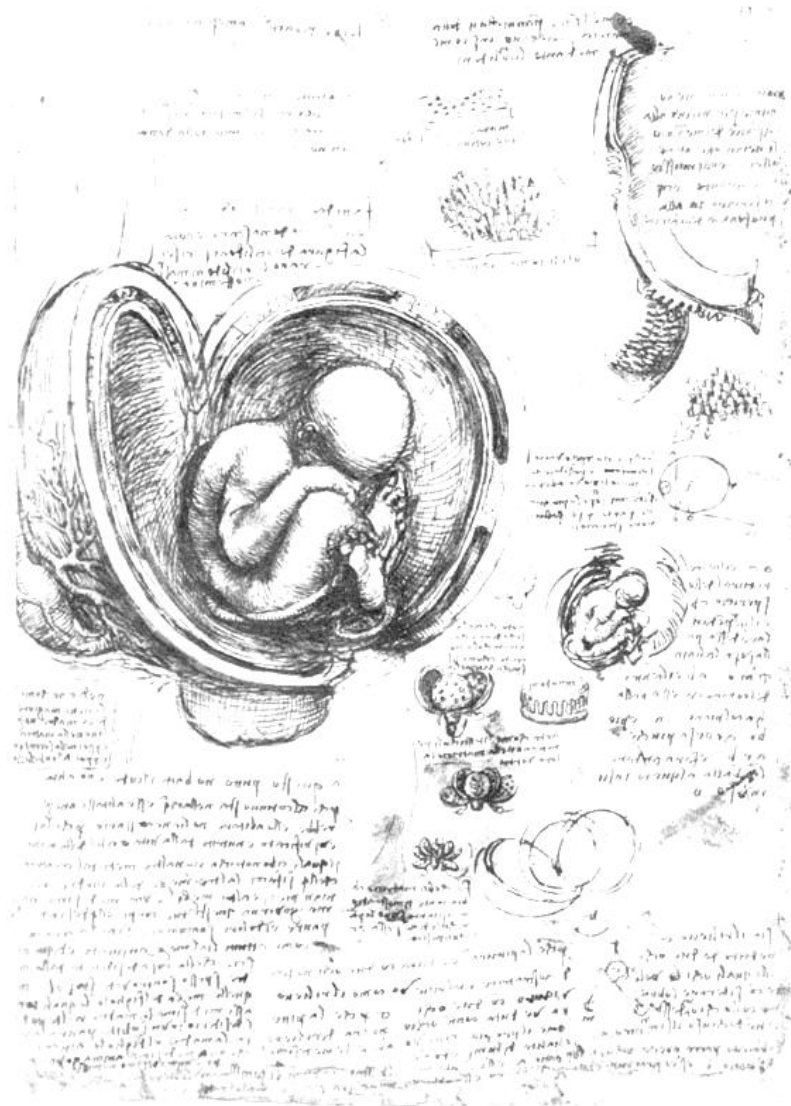


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# CONTENTS

## ARTICLES

CRISTINA FLOREA, ELENA ARDELEANU, ALEXANDRU CARABA SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS .....	219
ALEXANDRU F. CRIȘAN, VOICU TUDORACHE, OVIDIU FIRA-MLĂDINESCU, ALEXANDRU CRIȘAN, CRISTIAN OANCEA PULMONARY REHABILITATION DURING ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE NON-INVASIVE TECHNIQUES .....	230
MARIUS APOSTU, TRAIAN MIHAESCU UTILITY OF IPAG QUESTIONNAIRE IN EARLY DETECTION OF BRONCHIAL OBSTRUCTION IN PATIENTS WITH PULMONARY TUBERCULOSIS .....	239
HANS-JURGEN JAHRAUS, CRISTIAN MORNOS, CRISTIAN OANCEA, LUCIAN PETRESCU, ELENA ARDELEANU THE INFLUENCE OF BOSENTAN AND SILDENAFIL TREATMENT IN IMPROVING CLINICAL, ECHOCARDIOGRAPHIC AND LABORATORY PARAMETERS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION .....	249
GHEORGHE NINI, ADRIANA SOCACI, CONSTANTIN MARICA RISK ASSESSMENT FOR TB INFECTION IN A VULNERABLE GROUP IN AN ENDEMIC AREA .....	260
CRISTINA BREDICEAN, I. PAPA VĂ, CĂTĂLINA GIURGI – ONCU, R. ROMOSAN, Z. POPOVICI, M. ROȘU BIPOLAR DISORDER: FACTORS THAT INFLUENCE THEORY OF MIND .....	268
CĂTĂLINA GIURGI-ONCU, CRISTINA BREDICEAN, RADU ROMOSAN, ZSOLT POPOVICI, ANCA POPESCU PARTICULARITIES OF SOCIAL COGNITION IN THE DEPRESSIVE-DELUSIONAL PATHOLOGY .....	274

DAN SURDUCAN, DAN NEMES, MIHAI DRAGOI, RADU PETROMAN, EMA NADASAN, NORBERT GAL THE IMPACT OF COMPLEX ASSESSMENT ON THE EFFICIENCY OF INCIPIENT OSTEOSCLEROSIS DIAGNOSIS	280
GEORGE PUENEA, LILIANA CATAN, DAN NEMES, ELENA AMARICAI, DANIEL POPA, LAVINIA BUSESCU, ROXANA BALACESCU CHRONIC LUMBOSACRALGIA IN YOUNG ACTIVE ADULTS, A LIFESTYLE RELATED PUBLIC HEALTH PROBLEM?	286
RADU PETROMAN, DAN NEMES, MIHAI DRAGOI; DANIEL POPA COMPLICATIONS AND ASSOCIATED PATHOLOGY IN RHEUMATIC INFLAMMATORY DISEASES - A COMPLEX SPECIFIC AND INTERDISCIPLINARY APPROACH	291
N. POPESCU, G.A. POPESCU CONSONANTIST PSYCHOSOMATICS CONTRIBUTION OF DOCTOR ȘTEFAN ODOBLEJA TO THE PSYCHOSOMATICS CONCEPT	298
RADU-ȘTEFAN ROMOȘAN, TIBERIU MIRCEA, FELICIA ROMOȘAN, VIRGIL-RADU ENĂTESCU, BREDICEAN CRISTINA, CĂTĂLINA GIURGI-ONCU, LUCIAN ILE COGNITIVE-EMOTIONAL REGULATION STRATEGIES IN RECURRENT DEPRESSIVE DISORDER AND BIPOLAR DISORDER	304
N. NICULESCU, M. MUNTEAN, O. BORUGA, I. ZOLOG PREVALENCE OF DIABETIC RETINOPATHY IN BANAT DISTRICT	312
ADRIAN CAMEN, OCTAVIAN DINCĂ, TIBERIU NIȚĂ, CRISTIAN VLĂDAN, ALEXANDRU BUCUR A CASE OF MANDIBULAR CUNICULATUM CARCINOMA	320

<i>JIANU ALEXANDRU, ONISEI DOINA, STRATUL S.I.</i> CURRENT METHODS FOR IMAGISTIC EVALUATION OF ADULT PATIENTS WITH PERIODONTAL DISEASE UNDERGOING ORTHODONTIC TREATMENT. A REVIEW. PART II: RADIOGRAPHIC EVALUATION.	325
<i>LUPULESCU TEODORA EVA, COJOCARU HORIA, BERARI ADELINA RAMONA, PAȘCA PETRU CIPRIAN, ANGELA CODRUȚA PODARIU, URTILĂ EMIL, VOICU SEBEȘAN</i> EVALUATION OF THE KNOWLEDGE, SKILLS AND ATTITUDE OF A YOUNG ADULT TOWARDS THE PERIODONTAL DISEASE	334
<i>ALI FAHS, ANCA TEMELCEA, DANIELA MĂNUC</i> ESTHETICS OF THE SMILE IN ORTHODONTIC TREATMENT	341
<i>EZATOLLAH AGHAJANI, CRISTINA PĂDURARIU, BILAL TAKOUZLI, ANCA TEMELCEA</i> OBSERVATIONS ON THE IMPACTED MAXILLARY CANINE	345
<i>ANGELA CODRUTA PODARIU, MIRELLA ANGHEL, CRISTINA TALPOS, GEORGETA LUCIA BRINZAN</i> ROLE OF THE DENTAL HYGIENIST IN THE DENTAL PRACTICE	349
<i>CRISTIAN VLĂDAN, MIHAI BOGDAN BUCUR, NICOLETA MĂRU, OCTAVIAN DINCĂ, ALEXANDRU BUCUR</i> OSTEONECROSIS OF THE JAWS IN PATIENTS TREATED WITH BISPHOSPHONATES: AN UPDATE	353
<i>PASARIN TEODORA ADINA , MODJAHEDPOUR ESFANDIAR, TALPOS CRISTINA, LUCA MAGDA, BRATU ELISABETA</i> TREATMENT OF IMPACTED CANINES WITH A COMPLETELY CUSTOMIZED LINGUAL APPLIANCE. A CASE REPORT	358
<i>DENIS ȘERBAN , ANCUȚA BANU, COSTELA ȘERBAN, IOANA TUȚĂ-SAS, BRIGITHA VLAICU</i> ANALYSIS OF HEMOLYTIC BACTERIAL AEROSOL CONTAMINATION IN DENTAL PRACTICE	365

GOTIA SMARANDA LAURA, GOTIA SMARANDA RODICA, PODARIU ANGELA ORAL ENVIRONMENT IN STRESSFUL CONDITIONS .....	370
LIGIA VAIDA, ADRIANA PIRTE, ANCA PORUMB, RAMONA AMINA POPOVICI, ROXANA OANCEA, RUXANDRA SAVA-ROSIANU, CLAUDIA COREGA ASSESSMENT OF CHILDREN AND ADOLESCENTS' INTEREST IN PERSONAL APPEARANCE AND KNOWLEDGE ON ORTHODONTIC TREATMENT .....	378
MELINDA ONEȚ, ANGELA PODARIU, DANIELA JUMANCA, ATENA GALUSCAN, ROXANA OANCEA, RUXANDRA SAVA-ROSIANU, RAMONA POPOVICI CLASSIC VERSUS HYBRID DISJUNCTION THERAPY .....	389
ADRIAN BOLOS, CRISTINA MARIA BORTUN, MIRELLA ANGHEL, ION SILVIU BOROZAN, OTILIA BOLOS, VERONICA ARGESANU INVESTIGATION OF WORKING POSTURE AMONG DENTAL LABORATORY TECHNICIANS .....	393
ROXANA OANCEA, ANGELA CODRUȚA PODARIU, RAMONA AMINA POPOVICI, RUXANDRA SAVA-ROȘIANU, DANIELA JUMANCA, MELINDA ONEȚ CLINICAL ASSESMENT OF DIFFERENT METHODS USED FOR PROFESSIONAL DENTAL HYGIENE .....	399
RUXANDRA SFEATCU, ADINA DUMITRACHE, ANA PETRE, CONSTANTIN DĂGUCI, MIRCEA LUPUȘORU, NICOLETA MĂRU ORAL HEALTHCARE OF PRESCHOOL CHILDREN - STUDY OF PARENTS' KNOWLEDGE .....	406
LIANA SUCIU, CARMEN CRISTESCU, MELANIA BALAȘ, MIRELA VOICU, MARIA SUCIU, LIANA DRĂGAN, MIRELA TOMESCU THE COST-EFFECTIVENES ANALYSIS OF PERINDOPRIL VERSUS CANDESARTAN CILEXETIL TREATMENT IN HYPERTENSIVE PATIENTS WITH LEFT VENTRICULAR HYPERTROPHY .....	410

# SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS



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## ABSTRACT

*Systemic lupus erythematosus (SLE) is associated with an increased risk of accelerated atherosclerosis, many risk factors (traditional or lupus-associated) contributing to its development.*

*Aim: The aim of this study is to assess subclinical atherosclerosis by carotid ultrasound, as well as to characterise the responsible factors for the onset of atherosclerosis in SLE patients.*

*Material and method: The study has been conducted on 44 women, divided into two groups: SLE group (22 patients with SLE without renal pathology) and control group (22 healthy women of similar age). All the patients underwent carotid ultrasound, intima-media thickness (IMT) and atheromatous plaque presence being evaluated. Total cholesterol, triglycerides, C3, circulating immune complexes, antinuclear antibodies, blood pressure, and anti-double-stranded DNA antibodies were determined. SLE was characterised by: Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Systemic Lupus International Cooperating Clinics/American College of Rheumatology index (SLICC/ACR). Statistical processing has been performed by the means of Pearson and t-Student tests, with  $p < 0.01$  being regarded as statistically significant.*

*Results: Carotid IMT and atheromatous plaque incidence were higher in patients with SLE ( $p < 0.05$ ). In the SLE patients group IMT has been strongly correlated with: SLICC/ACR ( $r = 0.770$ ,  $p < 0.01$ ), length of disease evolution ( $r = 0.829$ ,  $p < 0.01$ ), systolic blood pressure ( $r = 0.765$ ,  $p < 0.01$ ). Medium correlations were recorded between IMT and diastolic blood pressure ( $r = 0.648$ ,  $p < 0.01$ ), number of relapses ( $r = 0.682$ ,  $p < 0.01$ ), total cholesterol ( $r = 0.569$ ,  $p < 0.01$ ).*

*Conclusions: SLE patients have a high incidence of subclinical atherosclerosis. The factors contributing to its onset are the traditional ones (dyslipidemia, hypertension, smoking), as well as those associated with lupus disease (evaluated by SLICC/ACR index).*

**Key words:** subclinical atherosclerosis, systemic lupus erythematosus

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## INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease associated with the production of a wide range of antibodies due to the loss of immune tolerance and onset of autoimmunity [1]. Despite the improvement of treatment schemes, both morbidity and mortality due to this disease remained high. Thus, even since 1976 Urowitz proposes a bimodal model for the mortality of SLE patients: while in the first years of evolution the mortality is due to disease activity or septic complications favoured by intensive immunosuppressive regimens, after five years it is frequently attributed to accelerated atherosclerosis [2].

Presence of accelerated atherosclerosis in SLE has been shown by Urowitz and colleagues [2], who described myocardial infarction in a 30 years old patient whose SLE evolved for more than 10 years. Later, many studies approached the issue of atherosclerosis and presence of SLE-associated cardiovascular diseases. It has been hence established that prevalence of clinical ischemic heart disease among SLE patients is of approximately 10% [3, 4].

Atherosclerosis has a long subclinical evolution. Detection of subclinical atherosclerosis is critical in order to apply methods to slow its progress and thus to avoid the onset of cardiovascular complications [5]. Endothelial dysfunction, the first step in atherosclerosis pathogenesis, was identified in SLE patients [6], while the carotid ultrasound showed the increase of intima-media thickness [7] on the one hand, and the presence of

atheromatous plaques on the other hand, in the absence of any symptomatology [8].

Identification of atherosclerosis lesions in young SLE patients, as well as the fact that up to 30% of deaths among SLE patients are due to coronary atherosclerotic disease showed that SLE is associated with an early-onset accelerated atherogenesis process. Traditional risk factors for atherosclerosis (dyslipidemia, diabetes mellitus, smoking, hypertension, obesity, hyperhomocysteinemia, early menopause, positive familial anamnesis for coronary disease, sedentariness) have a high incidence among SLE patient. However, even after these traditional risk factors have been controlled, high cardiovascular risk remains [3, 7, 9, 10]. There are hence cardiovascular risk factors strongly related to SLE: age at SLE diagnosis, chronic inflammation, circulating immune complexes, anti-endothelial cell antibodies, vasculitis, disease evolution time, secondary antiphospholipid syndrome, verrucous endocarditis, complement activation, chronic kidney disease, and high doses of cortisone administrated for long time [1, 7, 11].

Ultrasound evaluation of common carotid artery (intima-media thickness, presence of atheromatous plaques) is a non-invasive method to early detect atherosclerosis. The aim of this paper is to assess atherosclerotic lesions by carotid ultrasound, as well as to characterise the responsible factors for the onset of atherosclerosis in SLE patients.

## MATERIAL AND METHOD

The study has been conducted on 44 women, divided into two groups: SLE group (22 patients with SLE without renal pathology) and control

group (22 healthy women of similar age). All the patients underwent carotid ultrasound, intima-media thickness (IMT) and atheromatous

plaque presence being evaluated. Total cholesterol, triglycerides, C3, circulating immune complexes, antinuclear antibodies, blood pressure, and anti-double-stranded DNA antibodies were determined. SLE was characterised by: Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Systemic Lupus International Cooperating Clinics/American College of Rheumatology index (SLICC/ACR). Statistical processing has been performed by the means of Pearson and t-Student tests, with  $p < 0.01$  being regarded as statistically significant

The study has been conducted on 22 female patients with SLE, without renal pathology, having the disease for over one year. SLE diagnosis has been made based on ACR criteria revised in 1997. Drugs used by patients were Prednisone  $\pm$  Azathioprine. The control group has been composed of 22 healthy women of similar age.

Both groups underwent carotid ultrasound by the means of ALOKA ProSound 4000 echograph, using 10 MHz linear probe. Evaluation of carotid intima-media thickness (IMT) was done at 20 mm before common

carotid bifurcation (normal value  $< 0.5$  mm). Atheromatous plaque has been defined as focal thickening of vascular wall, with or without calcifications.

Biochemical and immunological investigation consisted in determination of: total cholesterol (Abbott photometry), triglycerides (Abbott reagent), anti-double-stranded DNA antibodies (Crithidia luciliae immunofluorescence), antinuclear antibodies (Hep 2 immunofluorescence), circulating immune complexes (EIA), C3 (Roche immunoturbidimetry).

SLE activity has been appreciated by the means of Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), while the degree of organic damage by Systemic Lupus International Cooperating Clinics/American College of Rheumatology index (SLICC/ACR).

Data were presented as follows: mean  $\pm$  standard deviation. Statistic analysis was performed by the means of Pearson (for correlation) and t-Student (for comparison) tests,  $p < 0.01$  being considered statistically significant

## RESULTS

The two groups (SLE and control) were similar regarding the age and the traditional cardiovascular risk factors. Diabetes mellitus, chronic kidney disease and secondary antiphospholipid syndrome were found in no patient (Table no. I).

Results of immunological explorations and SLEDAI and

SLICC/ACR values are presented in Table no. II.

A higher carotid IMT and a higher incidence of atheromatous plaques were recorded in SLE patients, as compared to the control group (Table no. III, Figures no. 1,2, 3).

Tab. no. I Comparative characteristics of the two groups studied

Parameter	Group	
	SLE	Control group
Age (years)	41,31818 $\pm$ 6,3349	35,02 $\pm$ 7,25
Duration of disease progression (years)	7,2727 $\pm$ 2,3539	0
Total cholesterol (mg/dl)	201,1818 $\pm$ 45,0107	204,4343 $\pm$ 43,45
Triglyceride (mg/dl)	142,1818 $\pm$ 36,5339	155,71 $\pm$ 25,87
Smoking (%)	27,27%	33,33%
Arterial hypertension (%)	50%	30%
Bloodpressure (mmHg)	136,8182 $\pm$ 17,76/82,5 $\pm$ 9,22	135,94 $\pm$ 9,99/80,75 $\pm$ 10,29

Tab. no.II Exploration results immunological indices SLEDAI, SLICC / ACR

Parametre	Value
Anti-double-stranded DNA (ui/ml)	0,001421±0,001048
C <sub>3</sub> (mg/dl)	68±12,20
CIC (µgEq/ml)	9,73±2,63
SLEDAI	10,81±3,45
SLICC/ACR	6,13±2,96
Number of relapses	2,63±1,43

Tab. no. III Carotid parameters of the two groups

Parametre	Group		p
	SLE	Control group	
IMT (mm)	0,73±0,20	0,58 ± 0,12	< 0,01
The presence of plaque (%)	36,36%	27,27%	< 0,01



Fig. no. 1 Carotid IMT in a control group



Fig. no. 2 Carotid IMT in a SLE group



Fig. no. 3 Carotid plaque in a SLE group



Carotid IMT in SLE patients has been strongly correlated with: SLICC/ACR ( $r = 0.770$ ,  $p < 0.01$ ) (Figure no. 4), disease evolution time ( $r = 0.829$ ,  $p < 0.01$ ) (Figure no. 5), systolic blood pressure value ( $r = 0.765$ ,  $p < 0.01$ ) (Figure no. 6).

Medium correlations were recorded between this parameter and diastolic blood pressure value ( $r = 0.648$ ,  $p < 0.01$ ), number of SLE relapses ( $r = 0.682$ ,  $p < 0.01$ ), and value of total cholesterol respectively ( $r = 0.569$ ,  $p < 0.01$ ). Carotid IMT has been weakly correlated with the values of triglycerides, C3, circulating immune complexes, anti-double-stranded DNA

antibodies, as well as SLEDAI. (Figure no.7, 8, 9)

Carotid IMT, as well as atheromatous plaques incidence had higher values in smokers than in non-smokers (Table no. IV).

Patients with atheromatous plaques had longer disease evolution time, higher SLICC/ACR compared to those without atheromatous plaques (Table no. V).

Patients treated exclusively with Prednisone (average dose 20 mg/24 hour) had greater intima-media thickness and higher atheromatous plaques incidence (Table no. VI).

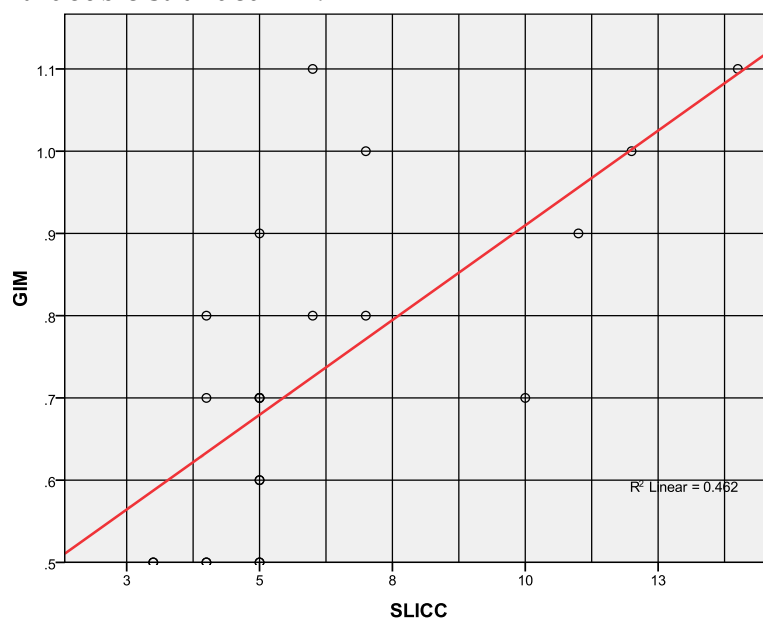


Fig. no. 4 Correlation between IMT and SLICC

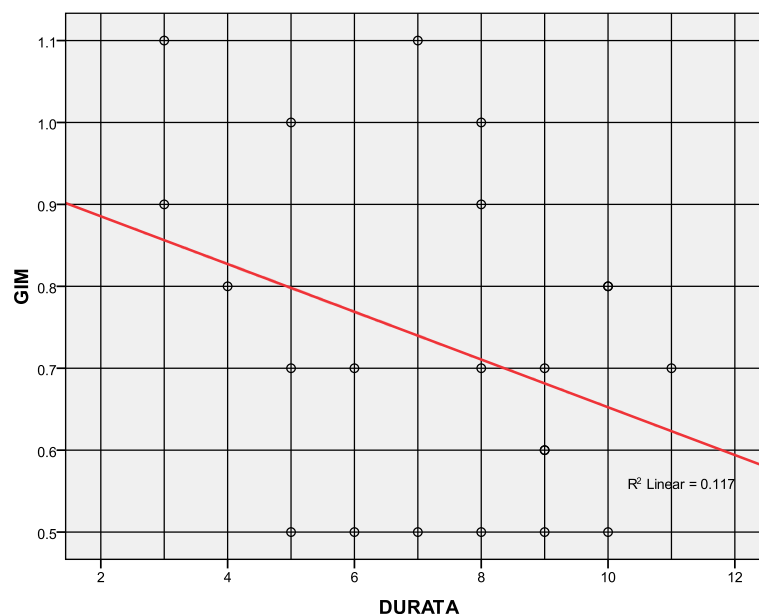


Fig. no. 5 Correlation between IMT and duration of disease

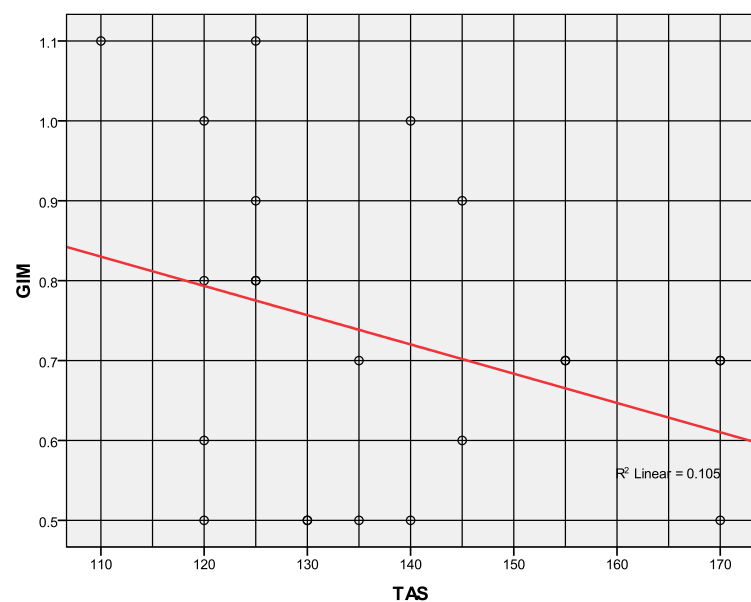


Fig. no. 6 Correlation between IMT and systolic blood pressure

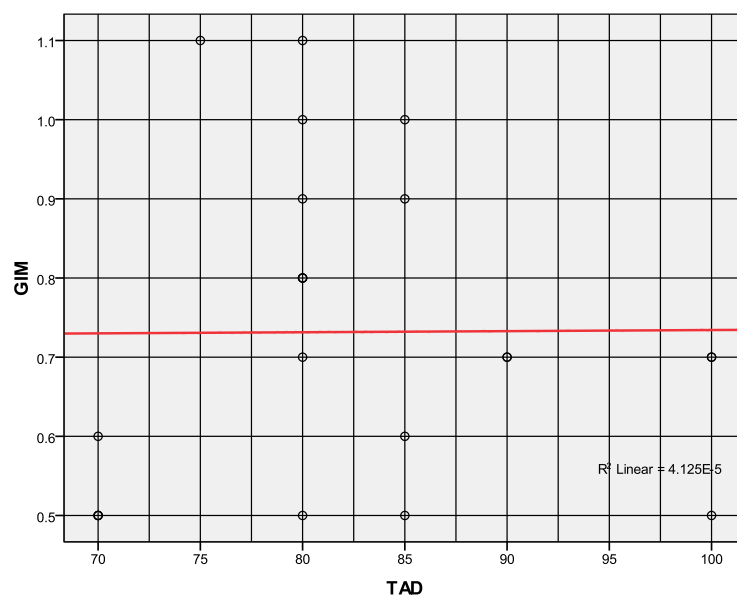


Fig. no. 7 Correlation between IMT and diastolic blood pressure

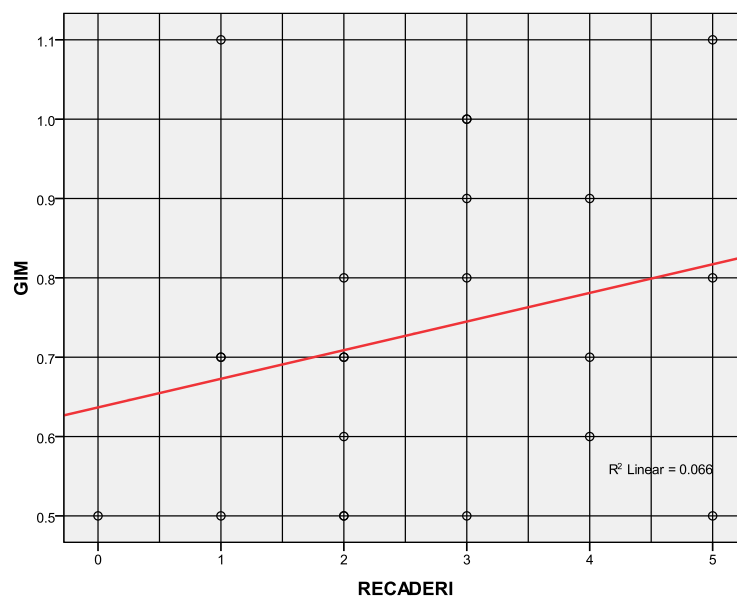


Fig. no. 8 Correlation between IMT and relapses

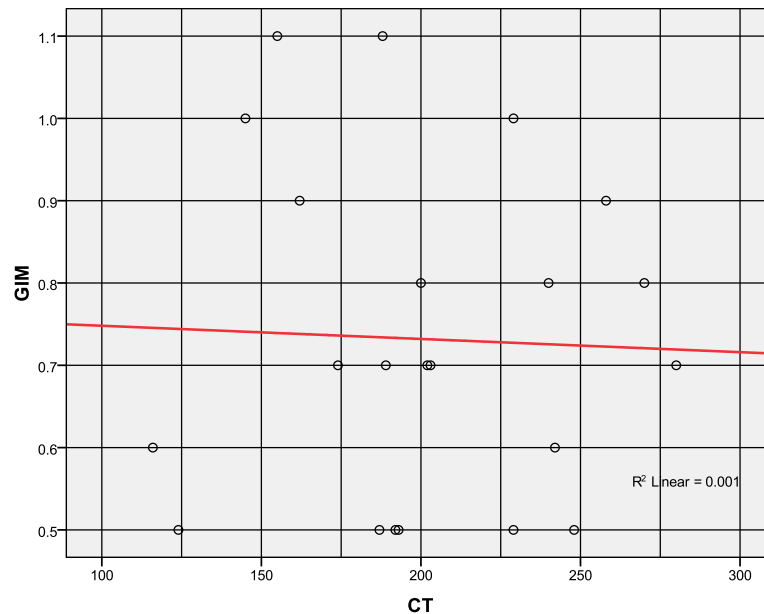


Fig. no. 9 Correlation between IMT and CT

Tab. no. IV Carotid parameters in smokers vs. nonsmokers

	Smokers	Nonsmokers	p
Number of patients	6	16	
IMT (mm)	0,744±0,22	0,72±0,18	< 0,01
The presence of plaque (%)	75%	37,5%	> 0,01

Tab. no. V Clinical and biological parameters in patients with carotid plaques

Parametre	Plaque		p
	Prezent	Absent	
Total cholesterol (mg/dl)	249,5±18,56	173,57±28,80	> 0,01
Systolic BP (mmHg)	128,75±8,34	141,42±20,23	> 0,01
Diastolic BP (mmHg)	90,62±8,21	77,85±6,11	> 0,01
SLICC/ACR	8,5±3,77	4,78±1,05	< 0,01
Duration of disease progression (years)	9±0,92	6,28±2,36	< 0,001
Number flares evolutionary	2,75±1,16	2,57±1,60	> 0,01

Tab. no. VI Carotid parameters according to the regimen used

Parametre	Treatment type		p
	Prednison	Prednison + Azatioprină	
Number of patients	10	12	
IMT (mm)	0,82±0,22	0,65 ± 0,15	> 0,01
Plaque presence (%)	62,5%	37,5%	> 0,01

## DISCUSSIONS

Systemic lupus erythematosus is a chronic inflammatory disease that affects mainly young women. Although therapeutic schemes have been significantly improved, thus increasing the survival time, both morbidity and mortality among these

patients remained high, chiefly because of cardiovascular diseases [11].

High prevalence of cardiovascular diseases at young ages is the consequence of an early extensive atherogenesis process [2, 12]. Non-invasive evaluation of subclinical

atherosclerosis patients by vascular ultrasound of common carotid artery quantifies two parameters: intima-media thickness (IMT) and atheromatous plaques presence [13].

Although the traditional risk factors are found also in SLE patients, they cannot explain the early accelerated atherogenesis process in them [3, 7, 9]. Currently it is considered that SLE is an independent risk factor for the onset of atherosclerosis by either characteristic immunological abnormalities or side effects of various drugs used [1, 8, 14]. Interaction between traditional and SLE specific risk factors explains early accelerated atherogenesis in these patients [15].

Carotid IMT has recorded higher values in SLE patients compared to controls, with statistically significant difference. De Leeuw [7] and Felea [16] found similar results, but their patients had lower mean value of carotid IMT ( $0.732 \pm 0.2$  mm). Atheromatous plaques prevalence in SLE patients is differently reported, ranging from 29% to 65.38% [8, 14, 17, 18].

Strong and medium correlations, respectively, have been recorded between studied carotid parameters and traditional risk factors for atherosclerosis: hypertension, smoking, total cholesterol.

Medium correlation ( $r = 0.569$ ,  $p < 0.01$ ) between IMT and total cholesterol value has been reported also by Jackson and colleagues [19]. Lipid profile in SLE is characterised by the increase of VLDL and LDL-cholesterol, as well as of triglycerides, along with the decrease of HDL-cholesterol. The process of lipid peroxidation takes place under chronic inflammation conditions, causing: direct endothelial injury, increase of platelet aggregation, increase of monocytes/macrophages recruitment and of LDL uptake by them, with the development of foamy cells, and induction of growth factors [20, 21].

Hypertension is one of the most studied traditional risk factors for

atherosclerosis, carotid abnormalities being correlated with the raise in blood pressure values [3, 8, 22]. In this study we have identified strong correlation between IMT and blood pressure values (Figure no. 6). Hypertension action in atherogenesis process is complex, increased blood pressure values causing endothelial dysfunction, changes in the biology of certain active substances in the vascular wall, LDL-cholesterol transport to the vascular wall [15].

IMT was higher in smokers, as well as the presence of atheromatous plaques, as compared to non-smokers. Smoking contributes to the onset of atherosclerosis by changing the lipid profile and by inducing a prothrombotic state [7].

The study of SLE-dependent parameters evidenced strong, medium and weak correlations with IMT and with the presence of carotid atheromatous plaques, respectively.

The strongest correlation has been recorded between IMT and SLICC/ACR index (Figure no. 4). The mean value of this index has been significantly higher in patients with carotid atheromatosis. SLICC/ACR index assesses tissue destructions in SLE evolution since its onset. Tissue damage is caused by both disease and treatment. Quantitative assessment of this index (in both active and inactive disease) is performed through 12 items: ocular, neuropsychic, renal, pulmonary, cardiovascular, peripheral vascular, gastrointestinal, musculoskeletal, skin damage, early menopause, diabetes mellitus, neoplasia (each damage should last for at least six months in order to be quantified) [23]. Thus, as the disease evolves, this index has an upward trend. Atherogenesis process is also gradual, the risk factors persistence inducing, and then worsening existing lesions. Similar correlations between carotid abnormalities and SLICC/ACR index have been described in other studies [8, 14].

Another strong correlation has been established between IMT and SLE evolution time (Figure no. 5), which can be explained by the fact that a longer evolution means: older age, higher cumulative Prednisone dose and risk of more evolutive attacks, leading to higher SLICC/ACR index [6, 14]. Atheromatous plaques have been also found in patients with prolonged evolution of SLE.

Emergence of an evolutive attack of SLE means important immunity disturbances, severe inflammation and higher doses of corticoids for its control. As atherosclerosis is strongly associated with inflammation, the greater the number of attacks, the higher the chances to develop atherosclerosis [14, 24].

Correlation between SLEDAI and carotid parameters was weak, without statistical significance, since this index mirrors the disease activity at a certain time (ultrasound performance time) [22]. SLEDAI value varies according to the response to treatment (relapses and remission, respectively) [25].

SLE is the classical model of disease caused by immune complexes. Although the immune complexes contribute to the onset of atherosclerosis through local inflammation and increase of cholesterol uptake by vascular smooth muscle cells, no significant correlations have been found between immune

complexes value, C3, anti-double-stranded DNA antibodies and carotid parameters, because these immunological markers vary during disease evolution [26, 27, 28]. As the immunological markers of inflammation vary over time, which is a consequence of post-therapy relapses and remissions, their value at a certain evolutive time does not correlate with IMT and the presence of carotid atheromatous plaques, respectively [29].

IMT and prevalence of atheromatous plaques were higher in patients treated exclusively with Prednisone (Table no. 6). Even though it has noteworthy anti-inflammatory effects, long-lasting high doses corticotherapy has many metabolic effects, out of which the most important is dyslipidemia. It has been seen that a Prednisone dose lower than 10 mg does not affect lipid metabolism, while a higher dose leads to the raise of cholesterol, B apolipoprotein and triglycerides levels [30]. High doses corticotherapy may interfere with atherogenesis by its effect on the traditional cardiovascular risk factors (dyslipidemia, hypertension, diabetes mellitus), which can be induced or worsened, as well as because this therapeutic approach involves the existence of an active severe form of SLE [20].

## CONCLUSIONS

Subclinical atherosclerosis has high incidence among patients with systemic lupus erythematosus. Besides the traditional cardiovascular risk factors, other factors related to the main disease, as well as to its treatment (assessment made by SLICC/ACR

index) occur in these patients. Vascular ultrasound of common carotid artery is a non-invasive mean to identify and quantify subclinical atherosclerosis in order to apply therapies to prevent the worsening of disease and the onset of clinically manifest atherosclerosis.

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# PULMONARY REHABILITATION DURING ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE NON-INVASIVE TECHNIQUES



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## ABSTRACT

Chronic obstructive pulmonary disease (COPD), a heterogeneous disease with increasing incidence, is one of the leading causes of death and invalidity worldwide and acute exacerbation is one of the main causes of hospitalization and premature death. Extensive data from literature about studies in which nasal and face-mask were used successfully to treat acute exacerbations of chronic pulmonary disease are reviewed. Most studies suggest that noninvasive ventilation (NIV) is superior to intubation and mechanical ventilation in acute exacerbations of COPD. Noninvasive positive-pressure ventilation (NPPV) is an effective treatment for selected patients with COPD, reduces dyspnea, prolongs sleep, improves partial pressure of arterial oxygen, and the quality of life scores in selected patients. Predictive factors for the use of NPPV with success in acute exacerbations of COPD and selection criteria for use of this method are analyzed.

**Key words:** chronic obstructive pulmonary disease, acute exacerbations, noninvasive ventilation, noninvasive positive-pressure ventilation, pulmonary rehabilitation

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disorder characterized by dysfunction of large and small respiratory airways and also by destruction of pulmonary parenchyma in varied combinations. The American Thoracic Society (ATS) defines COPD as “a preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The air flow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces significant systemic consequences”.[1]

Although COPD is a chronic disease, its evolution can be encumbered by appearance of

exacerbations, worsening of the symptoms of COPD (dyspnea, quantity and aspect of sputum) that last few days. The cause of exacerbation can be infectious (bacterial, viral or fungal) or it may be triggered by environmental pollutants or other factors. Generally, infections cause more than 75% of exacerbations; bacteria can be found in 25% of cases, viruses in another 25%, and both bacteria and viruses in another 25% of patients. Inflammation of airways is higher during exacerbations and so hyperinflation is increased, flow of expired air is reduced and transfer of gases is altered. These phenomena lead to hypoventilation and hypoxia, insufficient tissue perfusion and cellular necrosis.[2]

## PULMONARY REHABILITATION

Breathless is the most frequent symptom that limits exercise tolerance in patients with chronic obstructive pulmonary disease.

Pathophysiological factors that contribute to dyspnea caused by effort in patients with COPD include increased intrinsic mechanical loading of inspiratory muscles, i.e. the intrinsic positive end-expiratory pressure (PEEPi), the inspiratory threshold load (ITL), increased mechanical restriction of the thorax, weakness of inspiratory muscles, increased ventilator demand relative to capacity, gas exchanges abnormalities, dynamic airway compression, cardiovascular factors, and a combination of the above. Besides lung function, the force of peripheral muscles is also an important determinant of physical capacity in patients with COPD.[2]

Peripheral muscle wasting is a constant finding in cases with advanced COPD as well as in several other chronic diseases. Recent

advances in clinical research confirmed the negative impact of muscle wasting on patients survival rate and improved understanding how muscle mass is maintained. Consequences of peripheral muscle wasting on therapeutic approaches must be taken into account. Increase of muscle mass and strength are associated with better exercise tolerance and survival rate and so improving peripheral muscle force could be a reasonable therapeutic target in patients with COPD. Exercise limitation is an important consequence in COPD, which is marked in patients who require hospitalization. This fact is directly related to skeletal muscle weakness and quadriceps weakness is associated with increased mortality in COPD. Patients with low physical activity are more susceptible to be admitted to hospital and exacerbations lead to a dramatic reduction of physical activity and impairment of health status reflected in reduced time spent outdoors. Limited physical

activity is associated with a greater likelihood of relapse after discharge.[3,4]

In past times, patients with ARF were traditionally invasively treated, ventilated after endotracheal intubation. Sedatives and muscle relaxants were used to suppress spontaneous respiration and to facilitate mechanical ventilation. Today our understanding of pulmonary mechanics and pathophysiology is much better and we try to maintain spontaneous breathing as long as possible.

Dräger introduced the concept of biphasic positive airway pressure (BIPAP) ventilation in 1989 and created in 1995 the first ventilator that supported and stimulated spontaneous breathing during the entire respiration cycle in both volume and pressure controlled ventilation modes. In the effort to develop new protective ventilation strategies small tidal volumes and airways pressures below 35 cm H<sub>2</sub>O were used. Afterwards many studies demonstrated the benefits on gas exchange and alveolar recruitment with spontaneous breathing by BIPAP technique.[5]

Due to the fact that mechanical intrinsic workload and faulty performance of the inspiratory muscles contribute to breathlessness in COPD, assisted ventilation should provide benefits by lightening the burden of these overworked ventilator muscles.[13] Higher levels of training intensity may be achieved by reducing the effects of dyspnea felt during physical exercises with the aid of assisted ventilation. More studies have examined the acute effects of different methods of assisted ventilation over dyspnea and effort tolerance in severe cases of COPD. The results of these physiological studies can be resumed by the following: assisted ventilation provided either as non-invasive positive pressure ventilation (NPPV), CPAP or IPS, or proportional assisted ventilation (PAV), during physical

exercise it reduces dyspnea, eases the breathing activity and improves the effort tolerance in patient with COPD.[7,8,9]

Non-invasive ventilation (NIV) has been successfully used for the treatment of respiratory failure due to various causes, including sleep apnea, chronic obstructive pulmonary disease (COPD) and pulmonary edema. The Application of bi-level positive airway pressure (BiPAP), which associates pressure support ventilation with positive pressure, aims to increase the coefficient of alveolar ventilation during inspiration and to prevent alveolar collapse during exhalation.[6,7]

Later, intensive care physicians have begun to apply this non-invasive treatment to patients in critical stages in order to avoid intubation and to offer non-invasive support after intubation. Subsequently, many studies have shown that the use of NIV may reduce hospitalization in the intensive care units, as well as the frequency of nosocomial pneumonia associated with intubation.

Severe COPD places the respiratory muscles in a position of disadvantage. In emphysema, hyperinflation flattens the diaphragm increasing the radius of its curvature, accentuating the tension (according to Laplace's law) and increasing blood flow impedance. Even at the residual volume, the diaphragm remains flattened and the force that generates the inspiration is compromised due to the inability to get an optimal length of sarcomeres. In addition, the horizontal orientation of the ribs prevents the normal "bucket handle action" of the diaphragm on the chest, preventing the further expansion of the chest. Accessory muscles are recruited to maintain ventilation to the hyperinflated lung contributing to an already increased oxygen cost of breathing.[7,8]

Positive end-expiratory pressure (PEEP) is an additional workload

requiring the inspiratory muscles to decrease the pressure of alveolar sub-atmospheric level to initiate air flow for the next breath. During an exacerbation in COPD, a precarious situation could become catastrophic. Decreased inspiratory strength and lung elasticity, hypoxemia, or a combination of these factors increases the workload necessary for the respiratory process to take place, while the ability to provide that work is becoming more and more compromised. Exacerbations are often accompanied by worsening of alveolar hypoventilation, which leads to an increased number of breaths resulting in muscle fatigue. Often, in a futile attempt to compensate, the lungs become hyperinflated, relying even more on accessory muscles. Respiratory rate increases in response to the increased drive, shortening the expiratory time, and exacerbating auto-PEEP. This makes the breathing even more difficult, by adding inspiration to the imbalance between supply and demand for the effort of breathing. This becomes a vicious circle that leads to respiratory muscle fatigue, ventilatory failure and death unless the treatment interrupts the circle.[9,10]

Traditionally, there have been attempts to reduce respiratory resistance with the aid of bronchodilators, anti-inflammatory agents, careful oxygen supplementation and antibiotics. The traditional approach has often been effective, with the average rate of survival of 70% for patients with COPD treated with invasive mechanical ventilation for respiratory failure. However, the complications of invasive mechanical ventilation that occurred (including upper respiratory trauma, pneumothorax and nosocomial infections), were added to the morbidity and mortality. NPPV has been used for the treatment of COPD exacerbations, because it is an effective way to provide partially assisted ventilation while avoiding many complications of invasive mechanical

ventilation. When you combine applied PEEP to counteract the auto-PEEP and pressure support to assist the inspiration, NPPV reduces transdiaphragmatic pressure more than any applied PEEP or other pressure support on its own. Thus it has the potential to serve as a "crutch", while medical therapies need time to improve physiological defects and intubation can be avoided.[11,12]

CPAP and different ways of NPPV contribute to dyspnea reduction and help to increase effort tolerance for these patients. Relaxing the respiratory muscles and reducing the intrinsic PEEP have been considered main mechanism that stands on the foundation of these effects. Nocturnal home use of NPPV, beside a day by day rehabilitation program for patients that suffer of COPD severe has improved the effort tolerance and the quality of life.[9,10]

NIV can increase effort tolerance, can reduce desaturation induced by physical exercise and can help improve the obtained results through pulmonary rehabilitation for patients with chronic respiratory disease.

Using historically adequate data, Brochard was the first who has shown that ventilator pressure support through facial mask reduces significant the necessity of intubation, the duration of mechanic ventilation and the number of patients with exacerbation of COPD admitted in the intensive care units. Bott has reported significant improvements of PaCO<sub>2</sub> and dyspnea reduction in the first hour of using NPPV compared to the randomized control subjects.[12]

Kramer has proven after that NPPV reduces the endotracheal intubation rate to 9% instead of 67% for a subgroup with COPD patients. This study has also shown a faster improvement in the respiratory rate and in the blood gas values for the group treated with NPPV but did not show significant difference in the

number of hospitalization day or in the mortality rate.[12]

In a multicenter European study with 85 patients, Brochard has found that vital signs, blood gas values and encephalopathy score have improved more quickly in the NPPV treated group compared to the control group, intubation rate (74% vs. 26%), complication rate (especially pneumonia and endotracheal related complications), number of hospitalization days (35 days vs. 17 days) and mortality rate (31% vs. 9%) have been significant reduced for the NPPV treated group. In a smaller study, Celikel has found that NPPV has significantly reduced the intubation rate and the number of hospitalization days from 14,6 days to 11,7 days ( $p < 0,05$ ) compared with the control group.[12]

In a study using NPPV not just in academic medical centers (offering this way more relevant information for the "real world" application), Plant randomized 236 patients suffering of COPD exacerbation for the treatment with NPPV or with standard therapy administered by nurses in medical wards with respiratory profile. Intubation and mortality rate have been significant lower in the group treated with NPPV compared with the control group (15% vs. 27%,  $p < 0.02$ , and 10% vs. 20%,  $p < 0.05$ ) and the study has confirmed the former conclusions, faster and higher improvement of arterial pH, better respiratory rate and decreased dyspnea for the NPPV treated group. Mortality benefit was not apparent for the patients with  $pH < 7.3$  and the authors assumed that these subgroups with more severe diseases would have pursued better through close monitoring, such as in intensive care.[12]

Above mentioned studies have demonstrated that NPPV has a significant positive effect in exacerbation of severe and medium COPD, not just for improving rapidly symptomatic and psychological, but

also to reduce significant the need of intubation, complication, mortality rate and number of hospitalization days. More meta-analysis that combine have compared results in these studies have come to similar conclusions related to the mortality and intubation rate. In their meta-analysis, Keenan has found that NPPV was effective in treating exacerbations of COPD and reducing hospital costs by about 3,200 \$ compared with standard treatment. More recent Peter, has analyzed studies about NPPV effectiveness for ARF in general and found the greatest benefit in the COPD subgroup. The most recent meta-analysis performed by Lightowler, (in a systematic Cochrane review) and Keenan, has reported similar results about the use of NPPV for exacerbation of COPD patients. Both have found a significant reduction of the mortality rate (relative risk 0.41 reduction risk 10%) and the lower need for intubation (relative risk 0.41 reduction risk 28%). Further, both found a reduction of hospitalization days (-3.24 days and respectively -4.57 days) and Lightowler, found significant improvements of the  $PaCO_2$  and respiratory rate in the first hour for the group treated with NPPV compared with the control group. Furthermore, Keenan has found that these results can be demonstrated on patients with severe exacerbations but not on mild exacerbations. Based on these results, the meta-analysis authors and the participants of the consensus group believe that NPPV has to be used early in the course of an exacerbation of COPD. NPPV should be considered standard of care in cases of medium to severe exacerbations of COPD.[8,10,12]

More consensus groups recommend the use of NPPV in the treatment of COPD exacerbation. In 1997 at a respiratory conference it has been established to accumulate proof on the recommendation to use NPPV in the treatment of COPD exacerbation in the care units for acute patient, but

there are needs for more additional studies. In 2001 the International Consensus Conference on NPPV in the acute setting concluded that, the pathophysiology of conditions leading to hypercapnic ARF is amenable to interventions available within the context of NPPV, that there are physiological reasons for applying both inspiratory assistance and / or PEEP and that NPPV has the potential to reduce morbidity and mortality from possible hypercapnia respiratory failure.[12]

More recently British Thoracic Society (BTS) issued a consensus declaration on the use of NPPV for ARF. The declaration recommends that NPPV "should be taken in consideration for patients with exacerbation of COPD in which respiratory acidosis (pH lower than 7.35) persist despite maximum medical treatment with controlled oxygen therapy". Since 1990, NPPV has replaced negative pressure ventilation as an alternative to non-invasive ventilation for numerous advantages, including greater portability and convenience and the ability to treat obstructive sleep apnea. Investigators have estimated that NPPV would be better tolerated and more efficient than negative pressure ventilation in assisted ventilation for severe stable COPD patients.[12]

NPPV is safe and well tolerated for good selected patients. In both application of NPPV: acute and for long term, the most common problem encountered with patients with COPD is similar with the one from the other patients and is related to the mask or the air pressure. Patients often complain about the discomfort from the mask that could be attenuate by widening the gum that holds the mask or by trying to change different sizes or types of masks. For the acute application, patients can be anxious and can have difficulties synchronizing their breath with the machine. Changes in settings of the machine (increasing

or decreasing ventilator pressure, expiratory pressure titration to counter-balance the auto PEEP) and judicious using of sedative, improve synchronization.[11,12]

Another common cause is excessive air pressure that leads to sinus or ear pain, those can be attenuate by decreasing temporary the pressure and after increasing it gradual while tolerance is improves. Patients may complain of nasal congestion and dry mouth. For dry mucous membranes it is recommended to use nasal gel, air heating and the use of humidifier. For nasal congestion, inhalation of corticosteroids and decongestants or combinations of antihistamines are administered for improvement.

Other frequently encountered incidents: erythema, pain or ulceration of the nasal palate due to the air pressure from the mask, those can be attenuate by widening the mask, use of artificial skin or changing the mask with nasal pillows. Stomach insufflations are common, but are not critical, probably because the insufflations pressure is lower than the one used in invasive ventilation.[5,12]

NPPV has become an important component in the repertoire of the respiratory therapist (RT). During the initiation time with NPPV therapy the RT plays an important role. RT sustains and applies the necessary equipment for the NPPV treatment. The RT dedicates a considerable amount of time (for an hour or even more), in the progress of the first eight hours of NPPV, as compared to mechanic invasive ventilation. NPPV requires a team approach, with a medic who determines when NPPV is needed, nurses at least for acute states, provides continuous monitoring once NPPV is initiated. But the RT plays the critical role then when the NPPV is initiated making the patient cooperative and maintaining him with success in that state. Without qualified with experience RT, a NPPV program

cannot be implemented with success.[5,12]

A study that has been focused on investigating the effect of NIV on the effort tolerance for acute exacerbation of respiratory disease hypercapnia has shown that NIV given together with oxygen to patients has improved the "six minutes walking distance" (6MWD) by reducing the effect of dyspnea and improving the  $SO_2$  values, compared with exclusive oxygen therapy. Therefore, NIV brings an significant contribution to the lung rehabilitation in an acute episode, allowing patients to perform exercises that would otherwise be too dyspneic to continue and therefore to prevent the loss of strength and muscle functionality.[9]

Unlike previous studies, Van't Hul has used inspiratory pressure support (IPS) as a method of non-invasive positive pressure ventilation (NPPV). IPS is a form of mechanic ventilation, that can help the ventilation in a efficient way then when it is applied non-invasive to patients that suffer from chronic and acute respiratory failure. This is a pressure that is directed to each breath that is triggered and sustained by the patient. This offers ventilator support for each breath through the help of a positive inspiratory wave that is synchronized with the inspiratory effort of the patient. During the inspiration, airway pressure is raised to a preset: pressure level of support. This level is maintained until the machine determines the end of the respiratory effort of the patient or detects the need

of the patient to exhale. Previous researches have studied the effect of PAV supply during the workout. PAV is a way of partial assisted ventilation that has features of proportionality and adaptability to the intensity and duration of spontaneous ventilation mode by providing inspiration flow and pressure in proportion to the patient effort. The machine provides pressure according to the equation of motion, creating a pressure that is proportional to the spontaneous effort of the patient. A part from the total volume of the mechanic work, namely the elasticity and resistance, is taken in accordance with the machine support that was decided by the supervisor and can ease especially the resistance load and the elastic load.[8]

Non-invasive mechanical ventilation administered under the form of continuous positive pressure or pressional support ventilation (PSV), leads to the discharging of the respiratory muscles. Therefore mechanic non-invasive ventilation has found its use in severe exacerbation of COPD or in hypoxic respiratory failure. Also, it has been proven, that it leads to the improvement of dyspnea and effort resistance for patients with COPD. By using inspiratory support, it reduces the burden felt by the inspiratory muscles with a subsequent reduction of the respiratory effort. The blood gases circulation is improved and patients are able to support lactic acid for longer periods of time. Therefore, using ventilator support by PAV or PSV can increase exercise intensity.[7,12]

## CONCLUSIONS

Non-invasive ventilation increases significant the effort tolerance, in the same time reducing desaturation during physical exercise for patient hospitalized with exacerbation of chronic respiratory disease.

Pulmonary rehabilitation programs can be considered important instruments in the available therapeutic arsenal for COPD patients. The benefic effects of this type of intervention over the capacity of making effort, quality of life as well for symptoms, compared with standard

pharmacologic treatment or with pre-rehabilitation parameters are well known. In addition pulmonary rehabilitation has benefic effects over the pulmonary function, disease exacerbation and reduces the mortality.

Accumulated evidence and experience have shown that NPPV is playing an important role in the management of COPD exacerbation, decreasing remarkable the need of intubation, improving the results, including the decrease of mortality and complication rate and also reducing the number of hospitalization days. For COPD exacerbations, NPPV should be considerate standard treatment for the correct selected patients, and preferably used instead of invasive mechanical ventilation. NPPV can be used also in other situations for COPD patients: when respiratory failure overlaps with pneumonia, in post-operative respiratory failure, to facilitate extubation in order to reduce the complications of prolonged intubation, to avoid reintubation in patients who have failed after extubation and for patients who cannot

be intubated. To assure a good utilization of NPPV for these patients, selection guides are oriented to identify the patients who need assisted ventilation and exclude those who are too ill to use NPPV safe.

For severe stable COPD patients, current evidence suggests that NPPV can improve gas exchange during the day and night, can prolong the sleep, improve quality of life scores and possibly reduce the need of hospitalization. NIV utilization is expected to grow significant in the next years and clinicians, researchers and producers will have to collaborate together to gain more experience to face new challenges. Also, NIV can improve effort tolerance, resulting in decreasing desaturation for patients hospitalized with an exacerbation of chronic respiratory disease. The benefic action of NPPV over the recovery of the peripheral muscle is proved but for the results to have statistic value there are needed more subsequent cohort studies on a larger number of subjects.

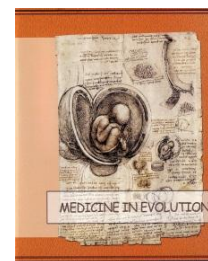
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# UTILITY OF IPAG QUESTIONNAIRE IN EARLY DETECTION OF BRONCHIAL OBSTRUCTION IN PATIENTS WITH PULMONARY TUBERCULOSIS



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## ABSTRACT

**OBJECTIVE** of the study is to evaluate the usefulness of IPAG (International Primary Care Airways Guidelines) questionnaire as a method of early detection of bronchial obstruction in patients with pulmonary tuberculosis (pulmonary tuberculosis).

**METHODS:** We evaluated the risk of COPD (chronic obstructive pulmonary disease) in patients with TB by filling out the IPAG questionnaire. The results were compared with those obtained by measuring lung function by spirometry or plethysmography.

**RESULTS:** There were analyzed the data of 84 patients with a mean age of 44.9 years, mainly from rural areas (61.9%) and mostly male (86.9%). According IPAG questionnaire, in the studied group 42.86% of patients had an increased risk of COPD, while 57.14% had no risk. Assessment of ventilatory function identified 41.67% of patients with normal functional parameters, 7.14% with obstructive ventilatory defect, 17.86% with mixed ventilatory defect and 33.33% with restrictive ventilatory defect. The data obtained show a high concordance between the two methods of assessment, 38.89% cases confirmed by spirometry with obstructive/mixed ventilatory defects had increased risk of COPD and 85.42% of cases without risk of COPD by evaluating suspicion questionnaire were with normal ventilatory function.

**CONCLUSION:** The use of tools as suspicion questionnaire may help early identification of patients with increased risk of developing obstructive ventilatory dysfunction, important in potentially contagious patients groups.

**Key words:** TB, COPD, questionnaire, early detection

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and pulmonary tuberculosis (TB) are two of the most common lung diseases with complex connections, relatively poorly known and relatively rarely approached in the specialized literature. Both TB and COPD are major public health problem worldwide, resulting in a huge burden on public health and health resources. The two diseases are widespread in Romania, covering a large part of pneumologists practice and concerns in our country.

Relations between TB and COPD are complex and bidirectional. They seem to have some similarities, both in terms of predisposing factors (smoking, pollution, poor socio-economic status), and clinical and functional layout (cough with purulent expectoration, exertional dyspnoea, bronchial obstruction).

The GOLD executive report 2006 shows that it is difficult to differentiate between COPD and TB in some cases, given the common respiratory symptoms and chronic obstructive airway flow in the two diseases. Therefore, the differential diagnosis of the two diseases should be considered, especially in developing countries where these affections are common [1].

COPD is a common comorbidity in tuberculosis (second in frequency after diabetes but before kidney failure, liver failure, or HIV infection-Human Immunodeficiency Virus) [2]. Inghammar et al. have studied the role of COPD as a risk factor for TB and found that patients with COPD, diagnosis certified by at least one hospitalization for this condition, have a three times higher risk of TB

compared to the general population. The risk of death in the first year after diagnosis of TB is two times higher in patients with COPD associated, compared with those who do not have this association [3].

Pulmonary TB is a risk factor for COPD. The GOLD report 2011 mentions that a history of TB may be associated with bronchial obstruction in adults over 40 [4]. Development of bronchial obstruction and respiratory signs may be preceded by one or more episodes of TB and it appears that the severity of the obstructive syndrome depends on the severity of the infection and radiological extension of tuberculosis lesions.

Obstructive symptoms (dyspnoea, wheezing, bronchial ronchus) are common in patients with TB, but are rarely investigated from epidemiological considerations.

Therefore, the simple tools of questionnaires of suspicion may be useful in identifying patients at risk of developing COPD and eliminating the risk of contamination of equipment in functional exploration services.

IPAG questionnaire (International Primary Care Airways Guidelines) contains eight simple questions and was designed and validated as a screening method for smokers over 40 years old to identify those at risk of COPD [5,6].

### OBJECTIVE

The objective of the study is to assess the usefulness of the questionnaire IPAG as a method of early identification of bronchial obstruction in patients with pulmonary tuberculosis.

## METHODS

There were included in the study inpatients with pulmonary TB in Pneumology Hospital Bacau.

Inclusion criteria: diagnosis of TB, according to the National Program for

Tuberculosis Control (NPTC), consent to participate.

A case of TB according to NPTC is a patient with TB confirmed bacteriologically or histologically, or patient with no disease confirmed, but where the pulmonologist has sufficient clinical and laboratory data to decide to begin TB treatment [7].

Exclusion criteria: refusal to participate; diagnosis of asthma and/or COPD spirometry documented; failure to perform a functional test technically acceptable; MDR TB.

We evaluated the risk of TB patients of developing COPD (obstructive or mixed ventilatory defect) by filling out the IPAG questionnaire (annex 1). The questionnaire was developed as a tool to identify patients at risk of developing COPD for family doctors in the UK [8]. A score  $\geq 17$  signifies an increased risk of COPD being present.

There were investigated smoking and nicotine addiction by classifying patients in smokers, former smokers and non-smokers. Tobacco use was quantified in number of packs-year (PA) for smokers and former smokers. Number of PA = (number of cigarettes smoked/day

$\times$  number of years smoked)/20. Nicotine dependence was calculated by

applying Fagerstrom test to active smokers (annex 2).

Evaluation of pulmonary function was done before discharge, after one month of treatment for patients with negative microscopic examination of sputum for identification of bacillus Koch (BK) and after sputum conversion (after 2-3 months of treatment) for patients with BK positive at microscopic examination. Lung function was measured by spirometry or body plethysmography and bronchodilator test. The spirometer used was a Jaeger Master Scope type. The body plethysmograph used was a Jaeger Master Screen Body type.

There were accepted tests that meet the criteria for acceptability and reproducibility.

#### Statistical analysis

In this research we used for statistical processing data the SPSS 17 program, dedicated to medical research. In the study were applied various tests, specific different types of data, of which we mention tests comparing mean values of a parameter corresponding to several groups of data including ANOVA, Scheffe, Spjotvol/Stoline, specific correlation tests for variables quantitative and qualitative variables, among which we can mention the Pearson, Chi - square ( $\chi^2$ ), Mantel-Haenszel, Fisher, Spearman, Kendall tau, Gamma.

## RESULTS

The study consisted of 84 patients, which were ward in the Pneumology Hospital Bacau, all confirmed with TB, according to NPTC criteria, and who have already started the appropriate treatment.

The average age of the patients was 44.9 years old, with a minimum of 17 and a maximum of 81.

The male gender was predominant, with a cover of 86.9 percent (73 of the 84 patients), while

the females represented only 13.1 percent (11 patients).

52 patients (61.9%) were from rural areas and 32 patients (38.1%) from urban areas.

The investigation of the smoking status resulted in having, out of the total of 84, 20 non-smokers (23.81 percent), 19 former smokers (22.62 percent) and 45 smokers (53.57 percent).

The level of nicotine addiction determined by the Fagerstrom test

revealed the fact that 13.3 percent of the smokers suffered of low addiction (7.14 percent of the 84 patients), 53.3 percent suffered of medium addiction (28.57 percent of the 84) and a percent just lower than 33 percent suffered of severe addiction (17.86 percent of the 84). (**Table I:** Results of the Fagerstrom test).

The evaluation of the ventilatory function found normal functioning parameters in 35 patients (41.67 percent) and ventilatory defects in 49 patients (58.33 percent).

After classifying the types of ventilatory defects, there have been identified 6 patients with obstructive ventilatory defect (7.14 percent), 15 patients with mixt ventilatory defect (17.86 percent) and 28 patients with restrictive ventilatory defect (33.33 percent). (**Table II:** Forms of ventilatory defects in TB)

Considering patients with OVD and MVD as a sole group of patients with obstructive phenomena associated with TB and evaluating their severity, we identified one patient with low dysfunction, 9 with medium dysfunction, 8 with severe defect and 3 with extremely severe defect. (**Table III:** The severity of bronchial obstruction in TB).

The analysis of the results regarding the score on the suspicion questionnaire revealed that 25 percent of patients presented a score lower than 19 and 50 percent of them a score lower than 15. (**Table IV:** Statistic indicators of the suspicion questionnaire's scores)

According to the interpretation of the scores on the suspicion

questionnaire, 42.86 percent of the patients presented a high risk of COPD, while 57.14 percent presented no risk. (**Table V:** Results regarding the risk of COPD)

The results show a high percentage of concordance of the two methods of evaluation: 38.89 percent of cases with OVD/MVD confirmed with spirometry present a high risk of COPD, according to the scores of the suspicion questionnaire, and 85.42 percent of cases with no risk of COPD present with normal ventilatory function. (**Table VI:** The correlation of the results of the suspicion questionnaire vs. the spirometry evaluation).

The analysis of correlation regarding the scores on the suspicion questionnaire for COPD compared to the spirometry evaluation showed a significant association ( $\chi^2=6.48$ ,  $r=0.576$ ,  $p=0.01052$ , 95 percent CI). (**Table VII:** The estimated parameters in the corelation of the scores of the suspicion questionnaire for COPD vs. the spirometry evaluation).

The analysis of the contingency table highlights the high chance of MVD/OVD in case of a positive result on the suspicion questionnaire (score  $\geq 17$ ), that being equal to 3.73 (OR=3.73). Prospective, the analysis allowed, through the rating of the relative risk, the evaluation of MVD/OVD risk in case of a positive result on the suspicion questionnaire, that being 2.67 times higher (RR=2.67). (**Table VIII:** The estimation of the risk parameters of COPD regarding the score on the suspicion questionnaire vs. spirometry evaluation)

Table I: Results of the Fagerstrom test

Fagerstrom test	No. of cases	% N=45 (smokers)	% N=84 (total)
Low addiction (score: 0-3)	6	13.33%	7.14%
Medium addiction (score: 4-6)	24	53.33%	28.57%
Severe addiction (score: 7-10)	15	33.33%	17.86%
<b>Total</b>	<b>45</b>		

Table II: Forms of ventilatory defects in TB)

Forms of ventilatory defects		No. Of cases	%
Normal pulmonary function (VN)		35	41.67%
Obstructive ventilatory defect (OVD)	medium	3	3.57%
	severe	3	3.57%
Total		6	7.14%
Mixt ventilatory defect (MVD)	low	1	1.19%
	medium	6	7.14%
	severe	5	5.95%
	extremely severe	3	3.57%
Total		15	17.86%
OVD+MVD		21	25%
Restrictive ventilatory defect (RVD)	low	3	3.57%
	medium	8	9.52%
	severe	12	14.29%
	extremely severe	5	5.95%
Total		28	33.33%
TOTAL		84	

Table III: The severity of bronchial obstruction in TB

Severity of obstruction	No. of cases	%
No obstruction	63	75.00%
Low obstruction	1	1,19%
Medium obstruction	9	10,71%
Severe obstruction	8	9.52%
Extremely severe obstruction	3	3.57%
Total	84	

Table IV: Statistic indicators of the suspicion questionnaire's scores

Average Suspicion questionnaire	Average		Std.dev.	Std.Er.	Min	Max	Q25	Median	Q75
	-95%	+95%							
15.43	13.89	16.96	7.08	0.77	4.00	38.00	10	15	19

Table V: Results regarding the risk of COPD

Score on the suspicion questionnaire	No. of cases	%
High risk of COPD Score of risk of COPD $\geq 17$	36	42.86%
No risk of COPD Score of risk of COPD $< 17$	48	57.14%
Total	84	

Table VI: The correlation of the results of the suspicion questionnaire vs. the spirometry evaluation

The evaluation of MVD/OVD		Spirometry		Total
		MVD/OVD present	MVD/OVD absent	
Score on the suspicion questionnaire	High risk of COPD	14	22	36
	Score of risk of COPD $\geq 17$	38.89%	61.11%	
	No risk of COPD	7	41	48
	Score of risk of COPD $< 17$	14.58%	85.42%	
		21	63	

Table VII: The estimated parameters in the correlation of the scores of the suspicion questionnaire for COPD vs. the spirometry evaluation

df=1	Chi- square $\chi^2$	P 95% confidence interval
Pearson Chi- square - $\chi^2$	6.481482	0.01090
Yates Chi-square	5.250000	0.02195
Corelation coefficient (Spearman Rank R)	0.5769231	0.01052

Table VIII: The estimation of the risk parameters of COPD regarding the score on the suspicion questionnaire vs. spirometry evaluation

	Estimated value	95% confidence interval	
		Minimum	Maximum
Odd ratio (OR)	3.73	1.18	12.13
Risk ratio (RR)	2.67	1.20	5.92

## DISCUSSIONS

COPD is a major cause of morbidity and mortality, being the fourth death cause, with a prospective of third death cause worldwide by year 2020. The escalation of mortality is caused by the expansion of tabagism and by demographic modifications and an increased percent of elderly population.

The diagnosis of COPD, although apparently effortless (association of cough and sputum production in patients over 40 years old exposed to risk factors, and bronchial obstruction evidentiaded by spirometry), is frequently tardy, mostly at a moment when the amputation of the pulmonary function is major. Bednarek et al. conducted a study on 1960 patients over 40 years old and identified 9.3 percent (183 patients) with COPD [5, 9]. Among these, only 18.6 percent have been previously diagnosticated. The author shows that a great number of new diagnosticated patients were symptomatic and necessitated treatment. Pena reports a prevalence of COPD of 9.1 percent in a study of 4035 subjects between 40 and 69 years old. Important is that 78.2 percent of the patients were newly discovered and aproximately half of those with severe forms of the disease were not receiving treatment[5,10].

The underdiagnosis and, consequently, the undertreatment for COPD is marked also in case of patients with TB. In our study, 25 percent of the patients suffered of OVD or MVD.

The necessity of an early diagnostic of COPD is a current debate topic. The effects of a pharmacological treatment on an asymptomatic patient are not very well known. Also, spirometry as a motivational tool in smoking reducing campaigns will have a low efficiency [5].

We still consider that is extremely important to identify as soon as possible all patients with ventilatory dysfunctions, especially because they become symptomatic too late, when FEV1(Forced Expiratory Volume in 1 second) drops below 50 percent of the predicted values. The early identification is even more important in case of patients with several risk factors, such as those who suffer of TB, usually smokers, paupers, facilitating quick interventions such as stopping cessation, pulmonary rehabilitation, respiratory function monitoring.

Specific to patients with TB and bronchial obstructive dysfunctions is, especially in early stages of antituberculous treatment, the posibility of contagiosity. This is why, often, the access to the classic method

of diagnostic, the spirometry, is prohibited or delayed. Accordingly, it would be important for the clinician to have at his use a simple tool of identification of patients with risk of COPD.

Using simple methods of screening in order to early detect COPD, such as the IPAG questionnaire, revealed itself as useful and reliable in primary medicine[5].

The IPAG questionnaire is based on 52 questiones, 8 of which are considered to be most predictable. The authors reported a sensibility of 80.4 percent and a specificity of 72 percent, making it appropriate for quick and accurate diagnostic of COPD [6]. Such an instrument could be useful in cases of patients with TB who can be suspected of COPD.

Sichletidis et al. shows that smokers with a score lower than 17 probably do not need a spirometry test, considering that the negative prediction of the IPAG at these patients is of 97 percent.

The results of our research are in conformity with this conclusion, as 85.42 percent of the patients who scored below 17 have normal ventilatory function. Also, an OR of 3.73 and a RR of 2.67 indicate that the IPAG questionnaire could be useful as a screening tool in detecting patients with TB at risk of developing COPD.

Obviously, ample and profoundly studies are necessary in order to validate such a questionnaire.

In conclusion, using instruments such as suspicion questionnaires can be helpful in early identification of patients with high risk of developing obstructive ventilatory dysfunctions, extremely important in groups of patients potentially contagious and for which access in laboratories for functional exploring could be difficult.

Early identification of patients with functional sequelae post-TB could help at inducing an active attitude towards them, supervision and prompt treatment, inclusion in anti-smoking or pulmonary rehabilitation campaigns.

# Anex 1

**IPAG** questionnaire for evaluating risk of COPD.

<b>Patient characteristic</b>	<b>Value</b>	<b>Score</b>
Age (years)?	40–49	0
	50–59	4
	60–69	8
	≥70	10
Smoking pack years?	0–14	0
	5–24	2
	25–49	3
	≥50	7
Body mass index?	<25.4	5
	25.4–29.7	1
	>29.7	0
Cough affected by weather?	Yes	3
	No or no cough	0
Sputum production in absence of a cold?	Yes	3
	No	0
Sputum production first thing in the morning?	Yes	0
	No	3
Wheezes?	Sometimes or often	4
	Never	0
Has or used to have any allergies?	Yes	0
	No	3
Total scores of ≥17 suggest increased risk of COPD being present.		



**Annex 2: Fagerstrom Test for Nicotine Dependence**

1. How soon after you wake up do you smoke your first cigarette?

After 60 minutes	(0)
31-60 minutes	(1)
6-30 minutes	(2)
Within 5 minutes	(3)
2. Do you find it difficult to refrain from smoking in places where it is forbidden?

No	(0)
Yes	(1)
3. Which cigarette would you hate most to give up?

The first in the morning	(1)
Any other	(0)
4. How many cigarettes per day do you smoke?

10 or less	(0)
11-20	(1)
21-30	(2)
31 or more	(3)
5. Do you smoke more frequently during the first hours after awakening than during the rest of the day?

No	(0)
Yes	(1)
6. Do you smoke even if you are so ill that you are in bed most of the day?

No	(0)
Yes	(1)

scor	0 – 3	Low dependence
	4 – 6	Medium dependence
	7 – 10	High dependence

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# THE INFLUENCE OF BOSENTAN AND SILDENAFIL TREATMENT IN IMPROVING CLINICAL, ECHOCARDIOGRAPHIC AND LABORATORY PARAMETERS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION



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## ABSTRACT

*Introduction:* Pulmonary arterial hypertension (PAH) represents a severe condition, with progressive evolution to death due to the deterioration of pulmonary circulation and of the right ventricular function (RV). *Aim of the study:* This study aims to analyze the impact of optimal bosentan and sildenafil treatment initiation in patients with PAH.

*Material and method:* We analyzed a lot of 38 patients with PAH. At the inclusion in the study, a first set of data was obtained including the clinical examination, surface electrocardiogram, pulmonary X-ray, standard biological samples, transcutaneous arterial saturation of O<sub>2</sub>, 6-minute walk test as well as right cardiac catheterization, conventional transthoracic echocardiography and tissular Doppler. Once completed the clinical and paraclinical tests within the evaluation protocol of the PAH patients, the treatment with bosentan and/or sildenafil was initiated according to the treating pulmonologist's decision.

*Results:* The group of patients was monitored at an interval of 3 months. After 9 months a full revaluation was performed. At a total of 17 patients (44.7%) readjustment of the initial treatment was necessary. At the end of the 9 months of monitoring, 15 patients were administrated monotherapy with bosentan (39.5%), 16 patients were treated with sildenafil (42.1%), and 7 patients received a combination of bosentan and sildenafil (18.4%).

*Conclusions:* Establishing an appropriate medical treatment had a beneficial effect on both the clinical and laboratory data. Optimal treatment leads to cardiac frequency, functional capacity of patients and transcutaneous saturation of O<sub>2</sub> reduction after 9 months of patients with PAH monitoring, compared to enrollment. A favorable evolution was also registered for echocardiographic data.

**Keywords:** pulmonary arterial hypertension, bosentan, sildenafil, conventional transthoracic echocardiography, tissular Doppler. **Key words:** subclinical atherosclerosis, systemic lupus erythematosus

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## INTRODUCTION

Pulmonary arterial hypertension (PAH) represents a severe disease, with progressive evolution to death due to the deterioration of pulmonary circulation and of the right ventricle function (RV). In most cases it is secondary, being the expression of a hemodynamic alteration of various etiologies and with different pathogenic mechanisms.

Pulmonary hypertension is defined as an increasing of the pulmonary arterial pressure  $> 25$  mmHg at rest or  $> 30$  mmHg at effort<sup>1</sup>. Death usually occurs by RV insufficiency or sudden death, in advanced stages. Since the conventional therapy has not given the expected results, in the recent years a number of new drugs acting in different ways<sup>2-3</sup> have been introduced: nitric oxide (sildenafil), endothelin (bosentan) or prostacyclin

(epoprostenol, treprostinil, iloprost). Although the optimal doses are not yet fully established, numerous clinical studies suggest the combination of two or even three drugs proven to reduce the systolic pressure in the pulmonary artery (SPPA)<sup>4-5</sup>, with the advantage of reducing pulmonary arterial pressure by exerting action on multiple pathways simultaneously. In our country, due to the very high costs, correct treatment of pulmonary hypertension is made in a limited number of patients who received the national health program which provides sildenafil and/or bosentan freely.

### AIM OF THE STUDY

This study aims to analyze the impact of optimal therapy initiation with this modern medication in patients with PAH.

## MATERIAL AND METHOD

We analyzed a group of 38 patients with PAH proposed for treatment with sildenafil and/or bosentan, in 2008-2012.

Inclusion criteria were represented by the following conditions: PAH with one of the following etiologies: idiopathic/familial; associated with connective tissue disease; associated with congenital heart defects of interatrial or interventricular septal defect type; patients with functional class NYHA II - IV PAH; patients in which the right cardiac catheterism shows an average pressure in pulmonary artery (aPPA)  $> 35$  mmHg, systolic pressure in the pulmonary artery (SPPA)  $> 45$  mmHg, pulmonary capillary pressure  $< 15$  mmHg; patients whose initially performed distance at the 6-minute walk test is  $> 100$  m and  $< 450$  m.

Exclusion criteria were represented by: inadequate echocardiographic window; PAH determined by obstructive or interstitial chronic pulmonary disease (except PAH associated with connective tissue diseases); portal hypertension; severe sleep apnea syndrome; electrostimulated rhythm.

At the inclusion in the study, a first set of data was obtained including the clinical examination, surface electrocardiogram, pulmonary X-ray, standard biological samples, transcutaneous arterial saturation of O<sub>2</sub>, the 6-minute walk test as well as the right cardiac catheterism. The severity of symptoms was evaluated based on subjective assessment of the patient, including the case in the functional classification WHO/New York Heart Association<sup>6</sup>: NYHA functional class I: no symptoms (fatigue or suffocation); NYHA

functional class II: no symptoms at rest, but symptoms in moderate physical activity; NYHA functional class III: without symptoms at rest, but symptoms in usual physical activity (dressing, bathing, walking, etc.); NYHA functional class IV: symptoms are present at rest, too.

In all the enrolled patients the surface electrocardiogram, standard postero-anterior thoracic radiography, conventional transthoracic echocardiography as well as the tissular Doppler were performed.

Echocardiography was performed by using Vivid 7 General Electric, Milwaukee, WI; the evaluation began with bi-dimensional examination and respectively in mode M determining of the diameter, surface and left atrial volume, telesystolic and telediastolic diameter of the left ventricle (LV), wall thickness of LV and RV, the telediastolic and respectively telesystolic volumes of LV, the RV diameter according to the current recommendations<sup>7</sup>. The amplitude of apical displacement of the tricuspid annulus (TAPSE) it was also determined in mode M from incidence apical 4 chambers. To calculate the ejection fraction (EF) of LV, the modified Simpson formula was used, based on the recorded images from incidence apical 4 chambers and respectively 2 chambers<sup>7</sup>, following the current recommendations. Subsequently the morphological appearance of cardiac valves was evaluated, and by overlapping the Doppler Color, pulsatile and/or continuous, the presence of valvulopathies has been documented and their quantification was achieved, as well. The pulsed Doppler transmitral flow was recorded from the apical 4 chambers incidence using a 3-5 mm sample volume placed in diastole between the peak of the mitral cusps, calculating the average of five consecutive cardiac cycles. A special attention was paid to obtaining an angle as reduced as possible between

the beam of ultrasounds and transmitral flow direction. The maximum early velocity (E wave) was measured during post-expiratory apnea<sup>8</sup>. The pulsed Doppler signal was recorded with a horizontal speed of 100 mm/s.

Doppler echocardiography allows accurate estimation of the SPPA and, thereby, it enables the diagnosis confirmation and grading of severity of PAH according to current guidelines.

For calculating the myocardial performance RV index Tei, time intervals of trans-tricuspid and respectively transpulmonary Doppler flow were used, from apical incidences and respectively short parasternal trans-aortic axis,<sup>9</sup>: "a" represents the time interval from the end till the beginning of the diastolic trans-tricuspid flow, and "b" the range from the beginning till the end of the systolic transpulmonary flow (respectively the ejection time). Tei index is calculated by the formula (a-b)/b. To achieve these measurements, the Tissue Doppler program of the device was set in pulsed mode. The motion of the mitral ring was recorded from incidence apical 4 chambers<sup>10</sup> within a frame rate ranging between 80 and 140 Hz. A 4-5 mm sample volume, positioned successively at the level of the septal and lateral extremity of the mitral ring, was used and later at the free extremity of the tricuspid ring. Two important negative waves were recorded during the diastole, due to the annular displacement toward the cord basis, one in the early phase (Ea wave) and another one during the late phase of diastole (Aa wave). Also, in systole a major wave (Samt) has been recorded during ejection, excluding isovolumetric phase, due to the displacement of mitral ring toward apex. Placing the sample volume at the free extremity of the tricuspid ring, a major wave (Satr) was recorded similarly with the mitral ring, during ejection, excluding isovolumetric phase, due to the displacement of

mitral ring toward apex. All the waves were recorded for five consecutive cycles during post-expiratory apnea and subsequently the arithmetic average of the found values was calculated. For the tissular Doppler recordings we used a horizontal speed of 100 mm/s. Starting from the obtained values, the E/Ea ratio was then calculated, using, for the velocities of mitral ring, the average of the two extremities, septal and lateral.

In all the enrolled patients the determination of arterial saturation of O<sub>2</sub> was performed, using the transcutaneous method and by arterial blood collection. Venous blood was drawn to determine hemoleucogram (blood count), transaminases, seric bilirubin, international normalized ratio, serum creatinine, serum ionogram. Afterwards these analyzes were monitored monthly.

The right cardiac catheterism was performed using as an approaching way the femoral vein. The invasive pressures were measured directly using some multipurpose catheters attached to a pressure transducer (Cordis Corporation, Miami, FL). The pressional data were recorded at the end of expiration, three consecutive cardiac cycles being stored and the average value (arithmetic mean) then calculated. The pulmonary vascular resistances were also determined, using the standard formulas. Echocardiography results were not known by the interventional cardiologist. PAH diagnosis was confirmed by right cardiac catheterism, invasive technique which documented the existence of an average pulmonary arterial pressure (aPAP) over 25 mmHg as well as a pulmonary vascular resistance higher than 3 Wood units.

Once completed, the clinical and paraclinical tests within the evaluation protocol of the patients with PAH, the treatment with bosentan and/or sildenafil was initiated according to the

treating pulmonologist's decision. The other drugs already included in the patient's treatment were given further if they did not have any contraindications to bosentan or sildenafil. Thus bosentan (Tracleer®; Actelion Pharmaceuticals, South San Francisco, CA, USA) was initiated with a dose of 2×62.5 mg/day per os, after 4 weeks the dose was increased to 2×125 mg to all patients in which increased hepatic enzymes were not noticed. In the sildenafil case (Revatio®; Pfizer, New York, NY, USA) the treatment was initiated at a dose approved by FDA for PAH treatment, of 3×20 mg/day per os. Following pulmonologist's indication, if after the first month, the results were not as expected, it was decided either to increase initial drug dosage, or the combination with the second.

The group of patients was monitored by the pulmonologist at an interval of 3 months. After 9 months a full reassessment was performed. If the case, the medication was readapted by the treating physician.

For the statistical analysis there were used specialized software SPSS 11.5 (SPSS Inc., Chicago, IL, USA) and NCSS 2004 (NCSS, Kaysville, UT, USA). Numerical variables are presented as average value ± standard deviation (DS) and compared using the t-Student or analysis of variations. The categorical variables are presented as absolute values or percentage and compared using the  $\chi^2$  test. The correlation between the different echocardiographic parameters was determined by Pearson correlation coefficient. The treatment effects after 9 months were compared with baseline data using the t-pair test. An inferior 0.05 P value was considered as being significant statistically. The study was approved by the Ethics Committee of the institution where the research was conducted; all the patients agreed to the inclusion in this study.

## RESULTS

Out of the 52 patients presenting PAH, only 38 could be included in the group of analyzed patients. The other patients were excluded due to exclusion criteria: inadequate

echocardiographic window (6 patients) and PAH caused by chronic obstructive pulmonary disease (8 patients). The PAH etiology in the studied group is presented in Fig. 1.

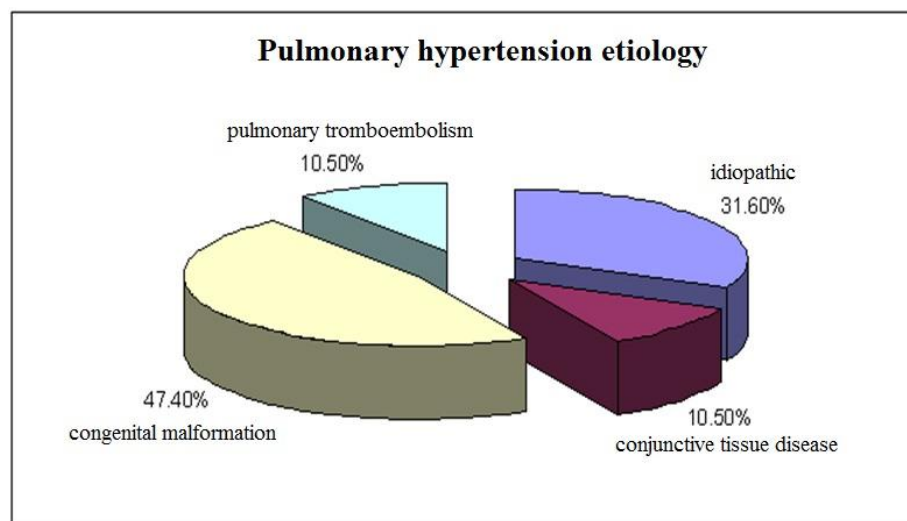


Fig. 1. Pulmonary arterial hypertension etiology in the patients included in the study.

The clinical characteristics of the patients at enrollment are presented in table 1. Echocardiographic parameters of the analyzed group at the time of

enrollment in the study are presented in table 2.

Table 1. Basic characteristics of the analyzed group (data are presented as average  $\pm$  DS or number (%))

Characteristics	Value
Mean age (years)	56 $\pm$ 17
Female/male	18 (47.4%) / 20 (52.6%)
Heart rate (beats/minute)	92 $\pm$ 14
Mean arterial blood pressure (mmHg)	104 $\pm$ 13
Functional class NYHA II	10 (26.3%)
Functional class NYHA III	15 (39.5%)
Functional class NYHA IV	13 (34.2%)
Body mass index (kg/m <sup>2</sup> )	26 $\pm$ 5
SPPA invasively determined (mmHg)	73 $\pm$ 8
aPPA (mmHg)	55 $\pm$ 11
Pulmonary vascular resistances (Wood units)	12 $\pm$ 5
6-minute walk test (m)	358 $\pm$ 76
Arterial saturation O <sub>2</sub> (%)	90 $\pm$ 6
Premedication: Diuretics	37 (97.4%)
Premedication: Calcium channel blockers	14 (36.8%)
Premedication: Digoxin	6 (15.8%)
Premedication: Acenocumarol	18 (47.4%)

Table 2. Echocardiographic parameters of the analyzed group at the time of enrollment in the study (data are presented as average  $\pm$  DS or number (%))

Characteristics	Value
Systolic pressure in pulmonary artery estimated SPPA (mmHg)	$70 \pm 11$
Diastolic pressure in pulmonary artery estimated DPPA (mmHg)	$37 \pm 8$
Ejection fraction LV (%)	$59 \pm 8$
Telediastolic diameter of left ventricle TDDVS (mm/m <sup>2</sup> )	$3.5 \pm 0.9$
Telediastolic volume of left ventricle TDVLV (ml/m <sup>2</sup> )	$75 \pm 18$
Telesystolic volume of left ventricle TSVLV (ml/m <sup>2</sup> )	$32 \pm 12$
Maximum amplitude of apical displacement of tricuspid ring in systole TAPSE (mm)	$14 \pm 5$
Left atrial volume (ml)	$41 \pm 12$
Pulmonary flow acceleration time (ms)	$68 \pm 11$
Tei index right ventricle	$0.49 \pm 0.09$
Maximum systolic velocity of the free extremity of tricuspid ring Sa <sub>tr</sub> (cm/s)	$8.7 \pm 2.8$
Maximum early diastolic velocity of transmitral flux E (cm/s)	$72 \pm 11$
Maximum early diastolic velocity of mitral ring Ea (cm/s)	$10.2 \pm 3.2$
E/Ea	$7.2 \pm 4.7$

The systolic pressure in pulmonary artery ( $70 \pm 11$  mmHg) estimated by the transthoracic echocardiography (through the systolic flow analysis of tricuspid regurgitation in Doppler continuous) presents an excellent correlation with SPPA determined invasively as shown in the simple linear regression ( $r=0.91$ ,  $p<0.001$ ); DPPA echocardiographic estimated using the pulmonary regurgitation flow has a value of  $37 \pm 8$  mmHg.

At a total of 17 patients (44.7%) was required readjustment of the initial treatment. Among the patients included in study, at the end of the 9 months of monitoring, a number of 15 were administrated monotherapy with bosentan (39.5%), 16 patients were treated with sildenafil (42.1%) and 7 patients received a combination of bosentan and sildenafil (18.4%)-Fig. 2. The average administered dose was 60 mg/day for treatment with sildenafil and 110 mg/day for bosentan respectively.

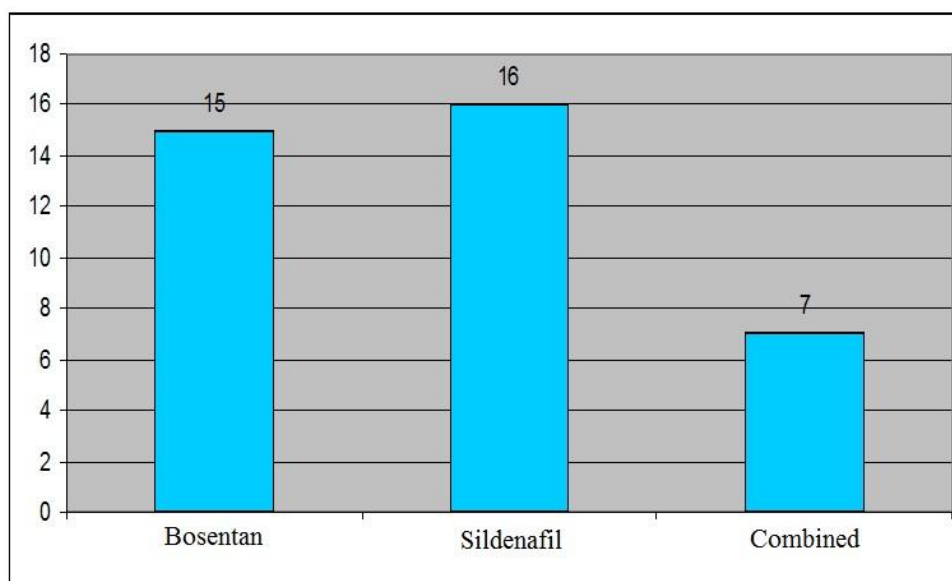


Fig. 2. The number of patients treated with sildenafil and/or bosentan at the end of the 9 months of monitoring



Establishing an appropriate medical treatment had a beneficial effect on both the clinical and laboratory data as well. The evolution of the tracked parameters during the treatment with sildenafil and/or bosentan showed at 9 months (compared to the enrollment time) reduction in heart rate ( $81 \pm 12$  vs  $92 \pm$

$14$  beats/minute,  $p < 0.05$ )-Fig. 3, improvement in the functional capacity of the patients (functional class NYHA-Fig. 4:  $2.6 \pm 0.7$  vs  $3.2 \pm 0.6$ ,  $p < 0.05$ ; 6-minutes walk test-Fig. 5:  $391 \pm 69$  vs  $358 \pm 76$  m,  $p < 0.05$ ) and transcutaneous saturation of  $O_2$  ( $93 \pm 5$  vs  $90 \pm 6\%$ ,  $p < 0.05$ ) also-Fig. 6.

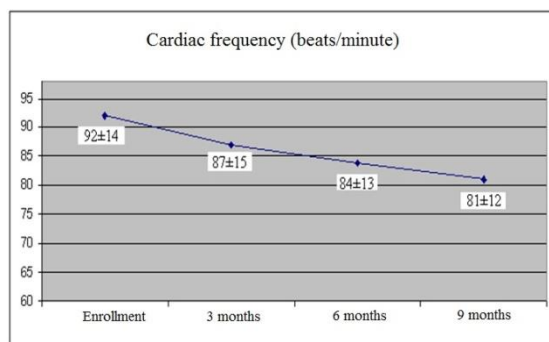


Fig. 3. Heart rate evolution during the 9 months of monitoring

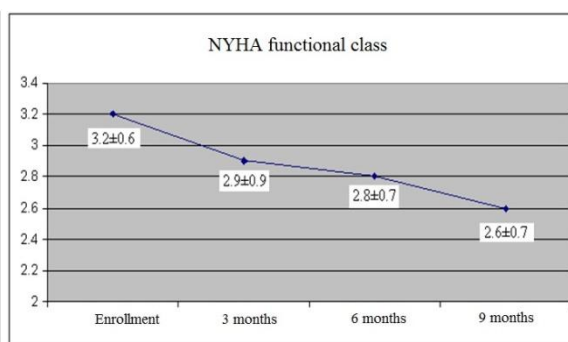


Fig. 4. NYHA functional class evolution during the 9 months of monitoring

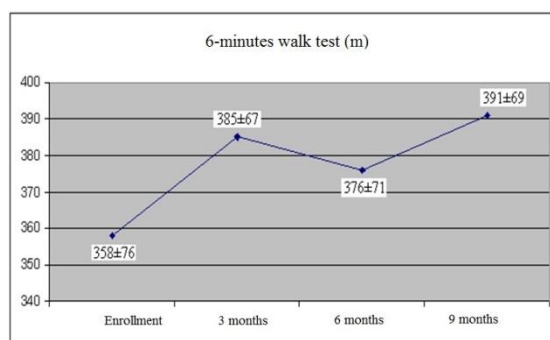


Fig. 5. 6-minutes walk test evolution during the 9 months of monitoring.

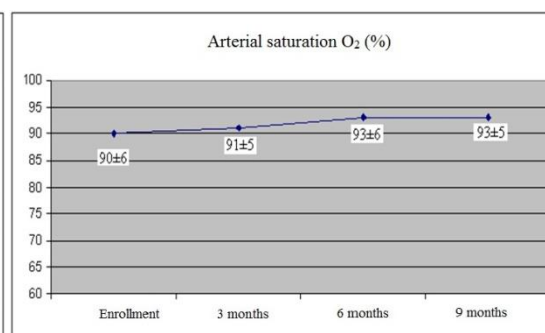


Fig. 6. Arterial saturation  $O_2$  evolution during the 9 months of monitoring.

A favorable evolution was also registered in the case of the conventional echocardiographic and tissular Doppler data: SPPA-Fig. 7 and PDAP-Fig. 8 estimated by ultrasound significantly decreased statistically ( $63 \pm 13$  vs  $70 \pm 11$  mmHg, respectively  $33 \pm 9$  vs.  $37 \pm 8$  mmHg,  $p < 0.05$ ), right ventricular function was significantly improved after treatment (TAPSE-Fig. 9:  $76 \pm 18$  vs  $75 \pm 18$  mm,  $p < 0.05$ ; Tei index-Fig. 10, calculated for the right ventricle:  $0.36 \pm 0.09$  vs  $0.49 \pm 0.09$ ,

$p < 0.05$ ; maximum systolic velocity of the free extremity of tricuspid ring Satr:  $10.1 \pm 2.1$  vs  $8.7 \pm 2.8$  cm/s,  $p < 0.05$ )-Fig. 11; on the other hand, the ejection fraction of LV, the telediastolic volume of left ventricle (TDVLV), the acceleration time of the pulmonary flow-Fig. 12, the early diastolic velocity of the transmitral flow as well as of the mitral ring, or the diastolic index E/Ea, although showing a trend of improvement, did not reach a level of statistical significance ( $p > 0.05$ ).

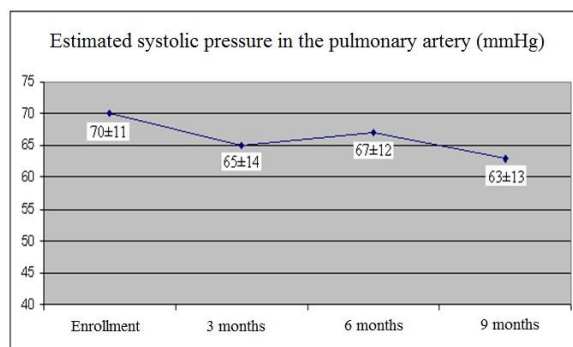


Fig. 7. Evolution of SPPA, estimated by echocardiography, during the 9 months of monitoring.

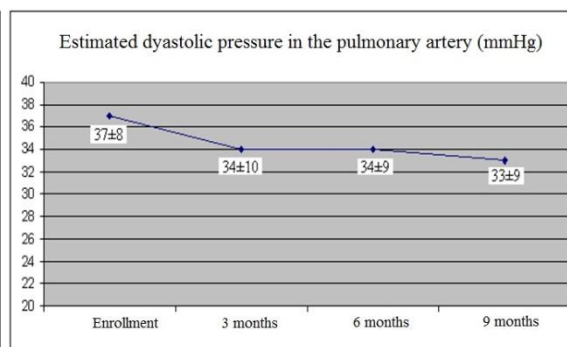


Fig. 8. Evolution of DPPA, estimated by echocardiography, during the 9 months of monitoring.

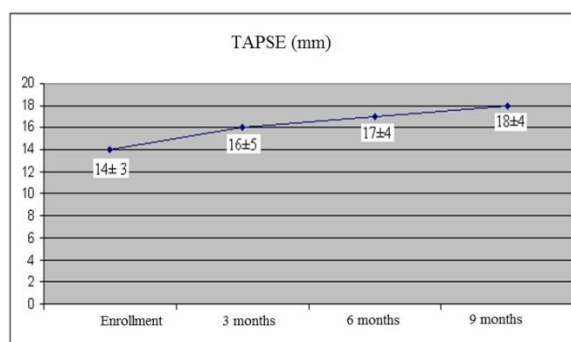


Fig. 9. Evolution of the maximum amplitude of tricuspid ring displacement, in mode M from apical incidence 4-chambers, during the 9 months of monitoring.

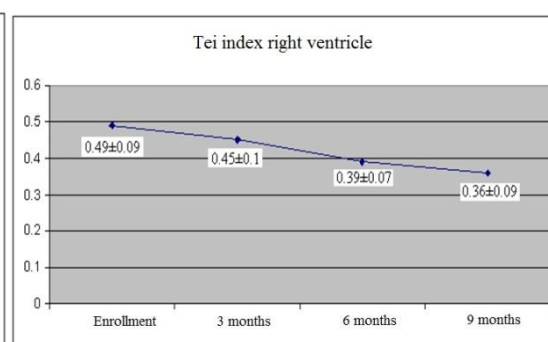


Fig. 10. Evolution of RV Tei index of myocardial performance, during the 9 months of monitoring.

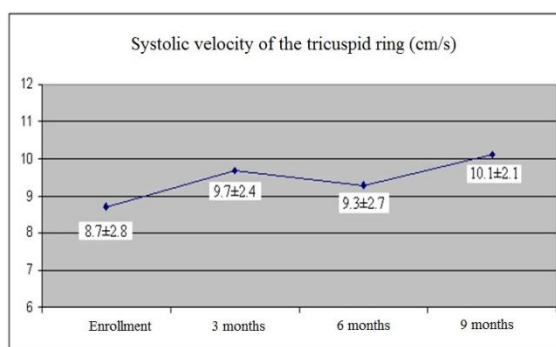


Fig. 11. Evolution of the systolic velocity of the tricuspid ring free extremity, during the 9 months of monitoring.

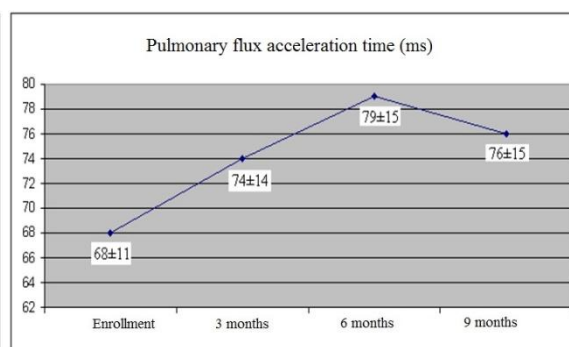


Fig. 12. Evolution of the acceleration time of pulmonary flow determined by echocardiography, during the 9 months of monitoring.

## DISCUSSIONS

This study documents that, in patients with pulmonary arterial hypertension, establishing an appropriate medical treatment has a beneficial effect on both clinical and laboratory data (including here the arterial saturation of O<sub>2</sub>, standard transthoracic echocardiography as well

as newer techniques, tissular Doppler). The best hospital readmission predictor was the 6-minutes walk test. Among the echocardiographic parameters, the best predictor of rehospitalisation, was represented by the systolic velocity of the tricuspid ring, obtained by tissular Doppler.

The optimal treatment determined in the analyzed patients a reduction in heart rate, in functional capacity (the functional class NYHA, 6-minutes walk test) and in transcutaneous saturation of O<sub>2</sub>, after 9 months of PAH patients monitoring (compared to enrollment).

In PAH, bosentan was studied in several main studies<sup>11</sup>: two studies on a total of 245 adult patients with diseases of functional class III or IV, either primary or caused by scleroderma, a study of 54 adults with PAH, class NYHA III, associated with congenital heart defects and a study of 185 patients with class II disease. The studies compared bosentan with placebo, associated to the patients' existent treatment. The main measure of effectiveness was the distance which the patients could walk in six minutes (a way to measure the capacity of physical activity), but the study for the class II disease also evaluated the resistance changes to the blood flow in pulmonary blood vessels. In patients with functional class NYHA II, bosentan reduced by 23% the vascular resistance, compared with placebo, after six months of treatment, but the distance that the patients could walk in six minutes was similar in the two groups.

The first double-blind trial, randomized, placebo-controlled, for sildenafil (SUPER-1-Sildenafil Use in Pulmonary Arterial Hypertension)<sup>12</sup> was performed on 278 patients with idiopathic, associated with collagen disease or repaired congenital systemic-pulmonary shunts PAH, the majority in the functional class II or III, in which sildenafil was administered (20, 40 or 80 mg three times/day) for 12 weeks. The increasing of distance in the 6-minute walk test with 45, 46 respectively 50 m, was demonstrated for the three doses, with improvement of the functional class and reduction of the mean pressure in the pulmonary artery without recording a significant decrease of the incidence of clinical

deterioration in comparison with placebo<sup>12</sup>.

Lunze et al were among the first who used this combination in the PAH therapy<sup>13</sup> and demonstrate the effectiveness in reducing transcutaneous saturation of O<sub>2</sub>, increase of the distance walked in 6-minutes walk test, the improvement of clinical status translated through the functional class NYHA as well as the reduction in arterial pressure invasively determined. The team of researchers led by Hoeper<sup>12</sup> has analyzed patients with idiopathic PAH showing improvement not only at the 6-minutes walk test, but also at the effort test. The same study reports the safety of association between bosentan and sildenafil.

A favorable evolution was also recorded in our study in terms of the echocardiographic data: SPPA and DPPA estimated echographically were significantly reduced statistically, the right ventricular function was significantly improved after the treatment (with improvement of TAPSE, of Tei index calculated for the right ventricle and Satr); instead, the ejection fraction of LV, TSVLV, the acceleration time of pulmonary flow, early diastolic velocity of the transmitral flow as well as of the mitral ring, or the diastolic index E/Ea, although showed a trend of improvement, did not reach a level of statistical significance. The transthoracic echocardiography is still an excellent way to detect the patients with clinical suspicion of pulmonary hypertension, for PAH confirmation, for grading its severity and assessment of consequences on the size and function of both ventricles. It currently represents the most widely used noninvasive imaging method for evaluating patients with PAH, both in the initial stage as well as in series, for assessment of the disease progression, of the prognosis and response to treatment. Improving of the conventional echocardiographic

parameters was reported in numerous studies that analyzed the effectiveness of different drugs for the management of PAH<sup>3,4,9,13</sup>.

To assess the systolic function of RV, TAPSE, Satr, and determination of myocardial performance index (Tei index) which represents the sum of isovolumetric contraction and relaxation times reported to the ejection time of RV can be used<sup>14</sup>. The value of this last parameter does not depend on the cardiac rate, on right ventricular filling conditions, the presence and degree of tricuspid insufficiency. The normal values quoted in the literature<sup>14</sup> are <0.28. Agapito and his collaborators<sup>15</sup> demonstrated the reduction of Tei index of the RV, following the establishment of an appropriate treatment of PAH in patients presenting Eisenmenger syndrome. Seyfarth has obtained same results on this new echocardiographic index in a

recent study conducted on patients with idiopathic PAH<sup>16</sup>. Another index recently introduced in echocardiography, easily obtainable, regardless the device, is represented by TAPSE. The normal values of TAPSE are >20 mm, and values <14 mm usually indicate a significant RV systolic dysfunction. The systolic velocity Sa of the tricuspid ring is significantly correlated with RV systolic function (estimated by measuring the change in area fraction of RV)<sup>17</sup>. It is considered that a maximum systolic velocity <11.5 cm/s expresses the RV systolic dysfunction with a sensitivity of 90% and a specificity of 85%<sup>18</sup>. In our study, all these parameters were significantly improved after 9 months of adequate treatment. On the other hand, both LVEF and LV diastolic function assessed using the ratio E/Ea did not change significantly after treatment.

## CONCLUSIONS

Establishing an appropriate medical treatment had a beneficial effect on both the clinical and laboratory data. The optimal treatment leads to a reduction in cardiac rate, in functional capacity of patients (functional class NYHA, 6-minute walk test) and in transcutaneous saturation of O<sub>2</sub> after 9 months monitoring of the patients with PAH (compared to the time of enrollment). A favorable evolution was also registered in the case of the echocardiographic data: SPPA and DPPA estimated

echographically were significantly reduced, right ventricular function was significantly improved after treatment (TAPSE, Tei index calculated for the right ventricle, Satr); on the other hand, the LV ejection fraction, TSVLV, the acceleration time of pulmonary flow, the early diastolic velocity of the transmitral flow and mitral ring, or the diastolic index E/Ea, although showed a trend of improvement, did not reach a level of statistical significance.

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# RISK ASSESSMENT FOR TB INFECTION IN A VULNERABLE GROUP IN AN ENDEMIC AREA



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## ABSTRACT

*The high incidence of tuberculosis (TB) in Romania is mainly due to the poor living standards, for at least part of the population nationwide, which also includes a large segment of the Roma population. At the same time, the newly diagnosed cases are just a small part of the cases with latent TB infection which represents a permanent source of infection for the general population. The only effective measure lies in identifying cases with latent infection and administering, when necessary, chemoprophylactic treatment that ensures that the patient no longer carries any infection and thus no longer poses the danger of developing the disease and spreading it to other individuals. For better specialised healthcare in the early diagnosing and monitoring of persons with a poor living standard, the current study aims at assessing the risk for TB infection in the Roma population in two rural areas in the West of the country (Arad and Timis counties).*

**Key words:** *vulnerable population, risk for TB infection, roma population*

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## INTRODUCTION

Tuberculosis (TB) remains a major public health issue worldwide as there are 8 – 10 million new cases and 1.7 deaths every year; besides, one third of the world population is infected with *Mycobacterium tuberculosis*.

In Romania, TB continues to be a high-impact disease despite all actions

carried out to implement the PNCT strategy. The western area of the country (Arad and Timis counties) is the region where the incidence of TB is still higher than anywhere in the country, especially within a segment of vulnerable population (the rroma)

## MATERIAL AND METHOD

The authors conducted a prospective study assessing the risk for TB infection in a group of rroma population living in the West of the country (Arad and Timis counties).

The target group consists of two Rroma communities living in the West of Romania, Sântana in Arad county and Sacoșul Turcesc in Timis county. The two villages were chosen because of the predominance of this ethnic group living there.

The information for the study was gathered using a questionnaire that focused on: the basic characteristics of the participants (gender, age), clinical characteristics (symptoms), history of the disease, socio-economical conditions.

The study group was selected based on the following criteria: persons who came into contact with a source of TB (patient with active pulmonary TB, patient who interrupted treatment or who did not respond to treatment), persons who had clinical symptoms of bacillary impregnation (irritating cough, asthenia, weight loss, sweating, sub-febrile state).

The persons selected according to the criteria above were examined clinically and were subjected to the

tuberculin skin test (TST) and chest X-ray.

The tuberculin skin test was carried out using the Mantoux technique which consists in intradermal injection on the ventral face of the forearm of 2 IU PPD (0.1 ml). A person who has been exposed to the bacteria is expected to mount an immune response in the skin containing the bacterial proteins, developing a palpable raised, hardened area of about 5 -6 mm in diameter which, if the injection was administered properly, looks like orange peel.

The test was interpreted 72 hours after injection (when induration is maximum and the non-specific reaction has already disappeared), and the transversal diameter of the indurated area was measured.

The test is considered positive if induration is:  $\geq 10$  mm in immunocompetent persons,  $\geq 5$  mm in immunocompromised persons (HIV/AIDS, immunosuppressive treatment, organ transplantation, etc).

The subjects who after chest X-ray showed alterations suggesting TB underwent further bacteriological exam in order to confirm/infirm the suspicion of TB.

## RESULTS AND DISCUSSION

The base profile of the study group was established depending of

the patients' area of origin (Arad or Timis) and the results of the TST

(positive or negative). The study comprised initially 1,539 participants, 73.6% (n=1,133) from Arad county (Santana), and 26.4% (n=406) from Timis county (Sacosul Turcesc). After

all the investigations had been carried out, 1,417 (92%) persons remained in the study group, divided as follows: 1,081 from Arad county and 336 from Timis county. (Fig. 1).

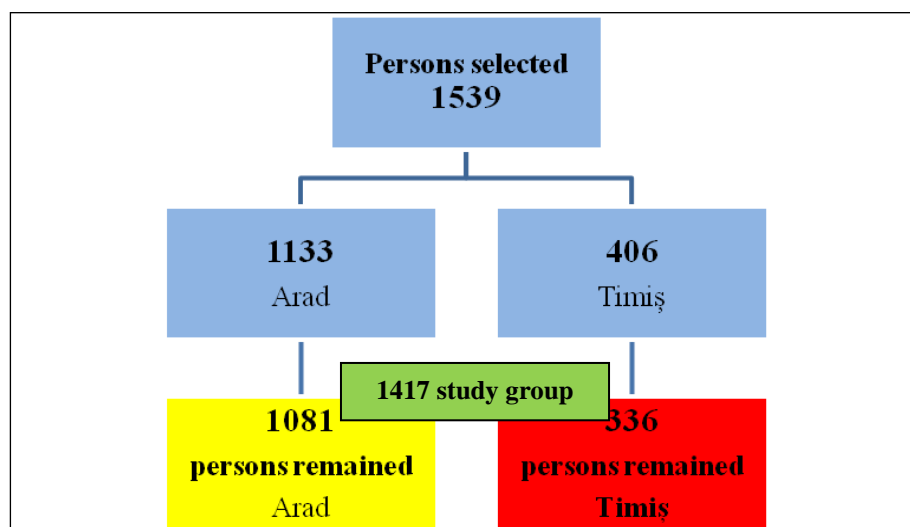


Fig. 1. Participants to the study

Gender distribution showed that 52% of the participants were male and 48% were female, and the predominance of male patients was significantly higher in the Timis county group (57% vs. 50% in Arad,  $p > 0.001$ ) (Fig. 2).

The age distribution shows a predominance of the group age 15 – 40

years, both in men and in women (Fig. 3).

The mean age of the study group was 29.5 years, in a non-homogeneous population. Of the total number of investigated persons (n=1,539), 75% were older than 19.

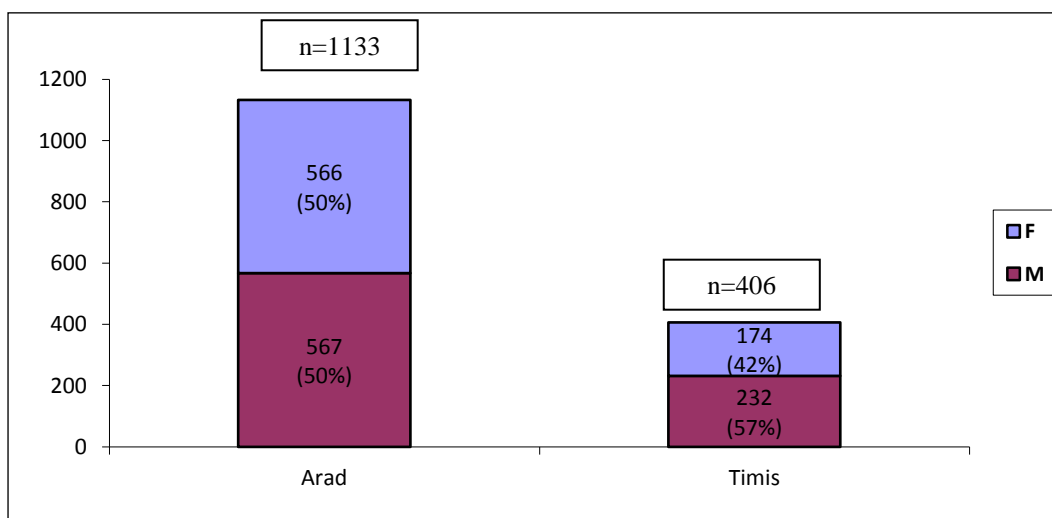


Fig. 2. Gender distribution of the study group/counties



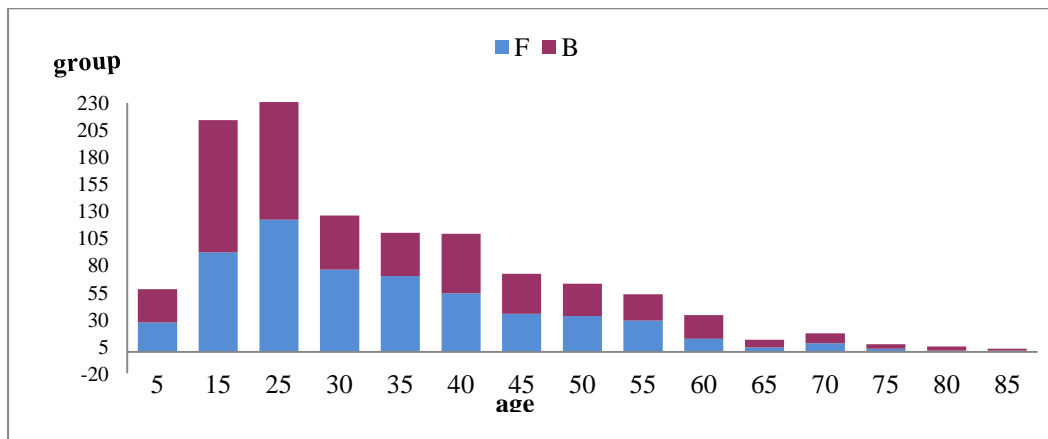


Fig. 3. Age distribution of the study group

The distribution of the study group according to the education of the subjects (Fig. 4) shows that more than half of the subjects (60%) have no education, 5% attended classes 1 – 3 of primary school, 20% completed primary school, 12% attended secondary school (gymnasium), and 3% of them finished high-school.

Out of the total number of adult persons, 26.6% had a permanent job, while 44.3% were unemployed, and 29.1% had day jobs. (Fig. 5). Only 15% of the subjects lived in families where the net monthly income/family member was > 150 lei.

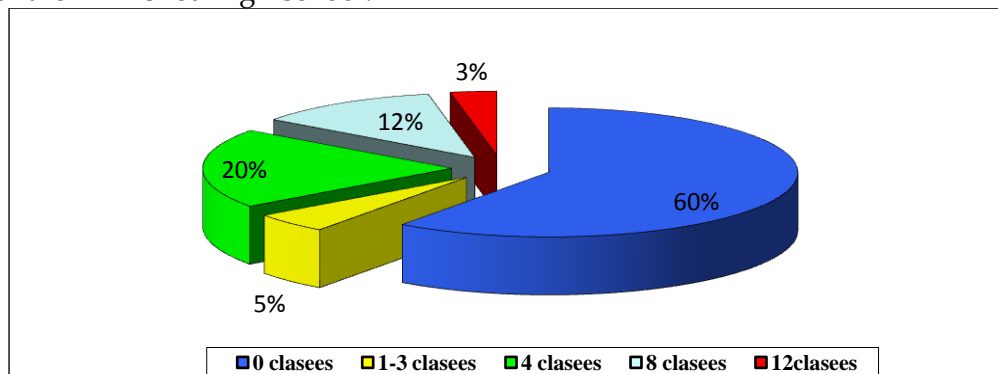


Fig. 4. Distribution of the subjects according to the level of education

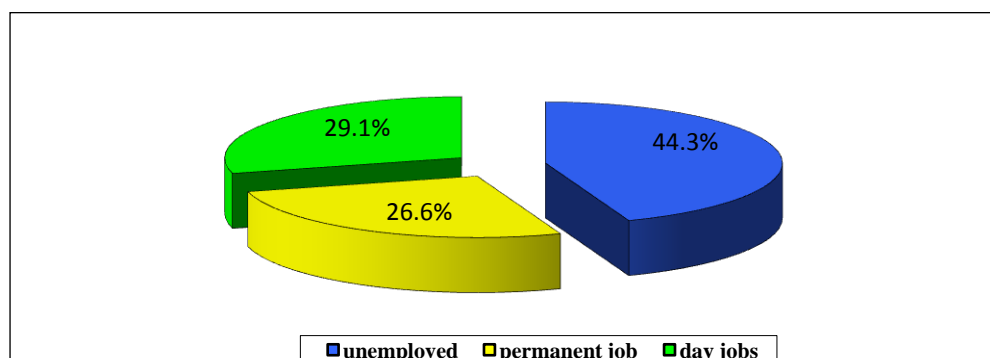


Fig. 5. Distribution of the subjects according to their work place

The average number of family members was 5.1, and 60% of the subjects lived in families consisting of more than five members. (Fig. 6). At the same time, only 2% of the participants live by themselves in one room, 39% share a room with another

person, 30% share a room with three other persons, while 19% share a room with four other persons. (Fig. 7).

A number of 1,417 persons (92% of the total number of subjects (n=1,539)) returned for a reinterpretation of the TST, as follows:

70.72% (n=1,081) from Arad county and 21.8% (n=336) from Timis county. (Figs. 8 and 9).

The diameter of the induration when interpreting the TST was: >10 mm in 31.3% (n=443) of the

investigated subjects, > 15 mm in 45.5% (n=645), <10 mm in 23.2% (n=329); none of the investigated subjects showed any signs of immunodepression. (Fig. 10).

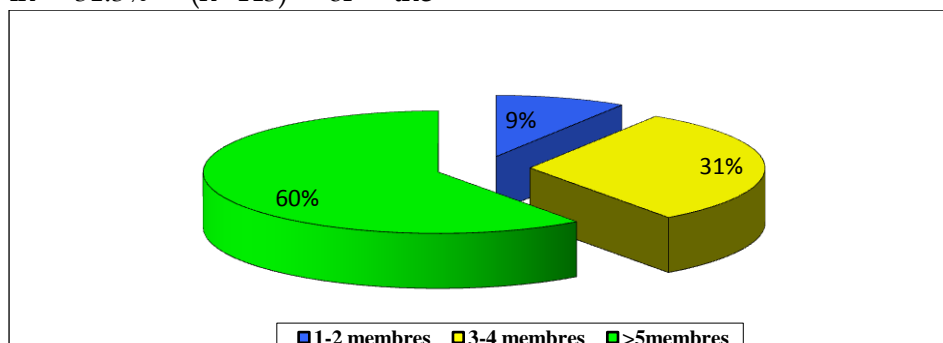


Fig. 6. Distribution of the study group according to the number of family members

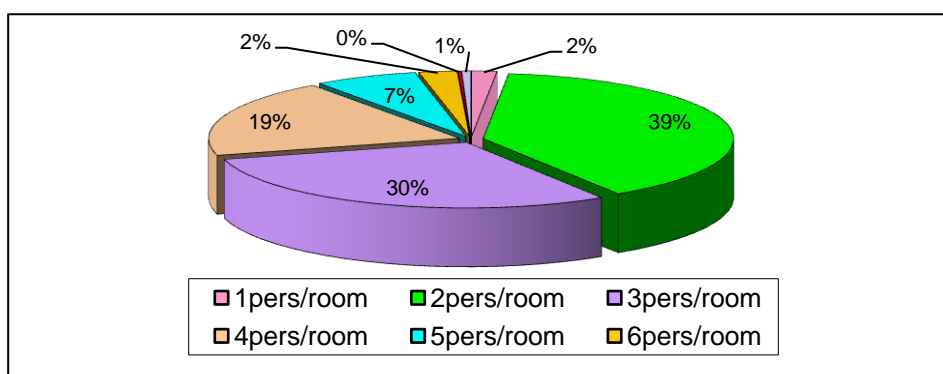


Fig. 7. Distribution of the study group according to living conditions

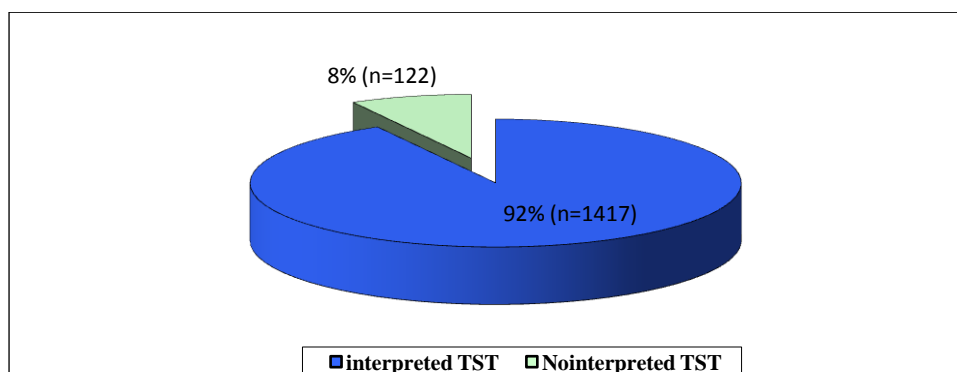


Fig. 8. Prevalence of the subjects whose TST was interpreted

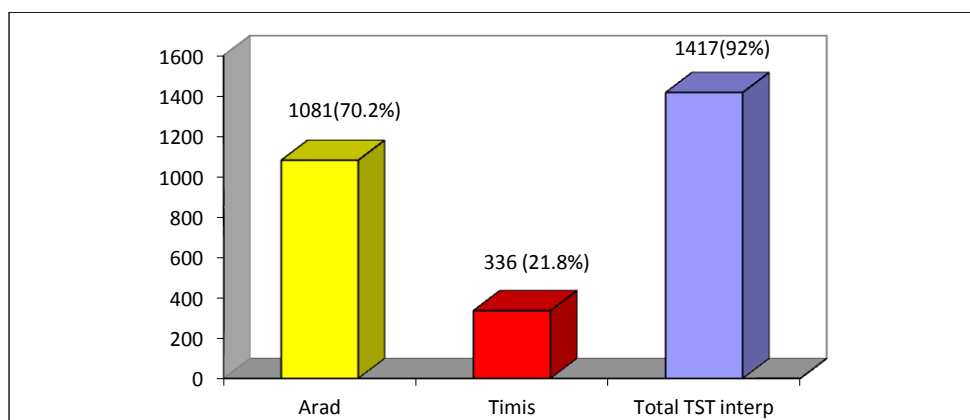


Fig. 9. Prevalence of the subjects whose TST was interpreted/study centre

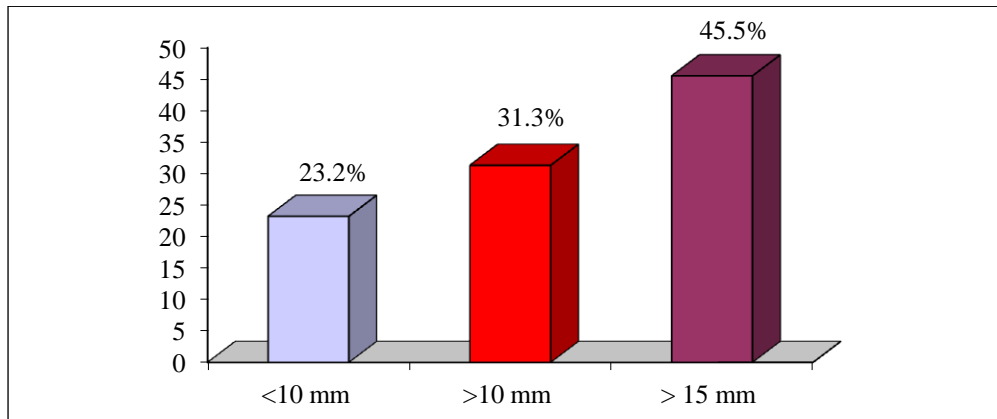


Fig. 10. The structure of the study group according to the results of the TST (mm)

The subjects with TST > 10 mm (76.8%, n=1,088) presented clinical symptoms suggesting bacillary impregnation: cough was present in 15% (n=163) of the subjects, nocturnal sweat in 14 % (n=152), weight loss in 15% (n=163). (Fig. 11).

Chest X-ray was performed for all the patients included in the study group (n=1,539), 45.5% (n=700) of which had non-specific alterations (severe interstitial aspect), and 54.5% (n=838) had normal radiological images

(NRI). (Fig. 12). Following the investigations and assessment of the subjects, 53% (n=817) subjects were diagnosed with latent TB infection (LTBI), 39% (n=600) of the subjects did not require specific prophylactic treatment (being labelled as follow-up cases), and 8% (n=122) of the cases were considered as “lost” as their investigations were not finalised (the subjects did not show up for the interpretation of the TST). (Fig. 13).

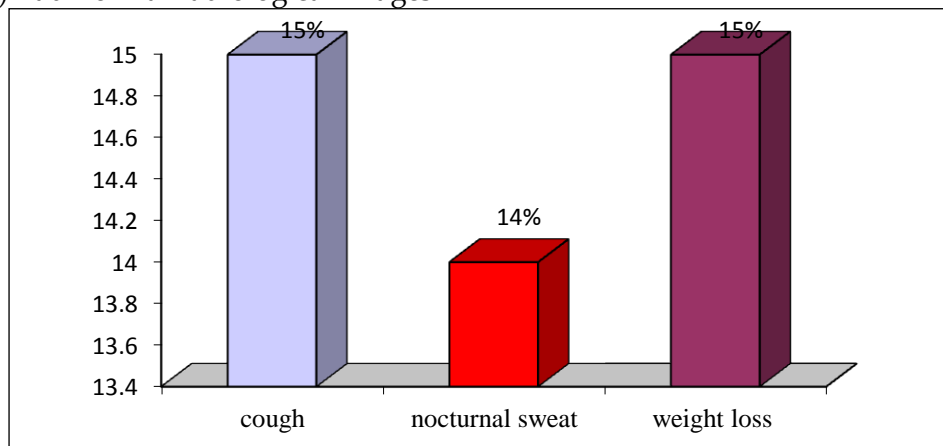


Fig. 11. Clinical symptoms in patients with TST >10 mm

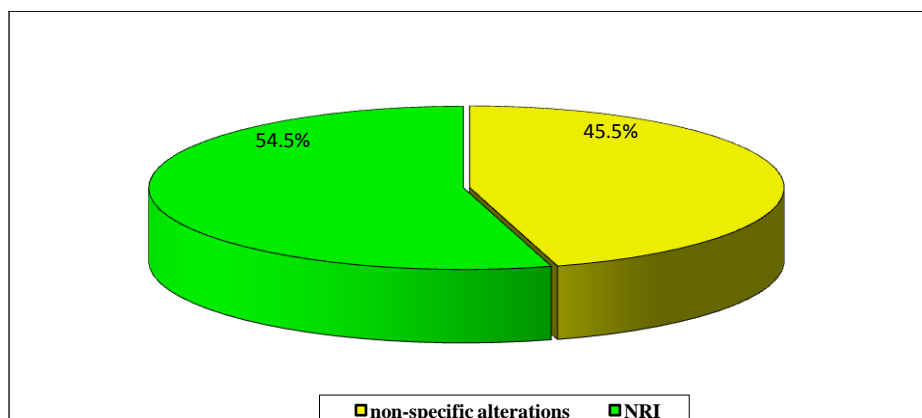


Fig. 12. Distribution of the study group according to the results of the chest X-ray

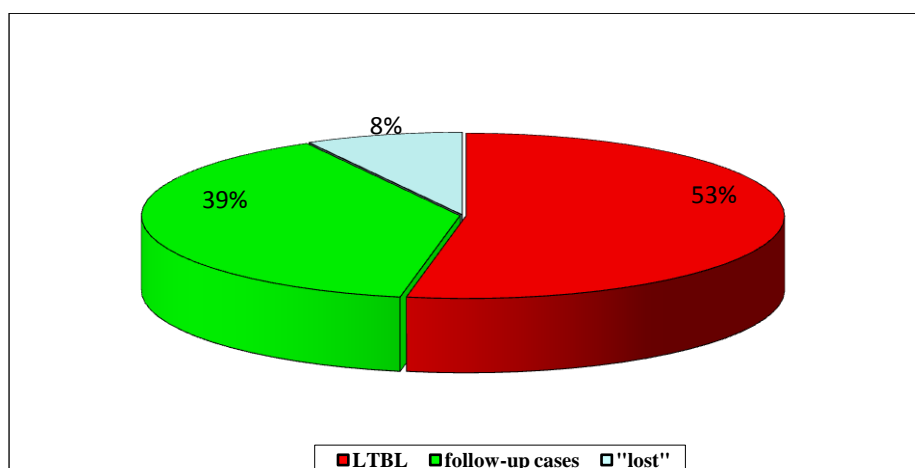


Fig. 13. Prevalence of LTBI in the study group

## CONCLUSIONS

Based on the socio-economical and educational levels of the investigated adult population, the study concluded that the two communities represent vulnerable groups to disease in general and for TB in special, due to the following reasons:

- sixty per cent of the subjects hadn't even finished the first year of primary school and only 2% had finished high-school;
- the average number of family members was 5.1, and 60% of the participants belonged to families that consisted of more than five persons;
- only 15% of the subjects included in the study lived in families with a net average income/family member > 150 lei;

- only 2% of the subjects had a room only to themselves, while 30% shared a room with at least three other persons and 19% shared a room with at least four other persons;

- only 26.6% of the adult subjects declared having a stable job.

Considering that 53% of the subjects had LTBI, being therefore infected with *Mycobacterium tuberculosis*, we recommend the use of TST as a means of diagnosing TB infection, alongside clinical symptoms and  $\pm$  chest X-ray.

At the same time, considering the fact that few subjects had a permanent job, we recommend a recurring screening of the population of the two villages as a means of early diagnosis of TB.

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# BIPOLAR DISORDER: FACTORS THAT INFLUENCE THEORY OF MIND



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## ABSTRACT

*In the last years evaluation of ToM (Theory of Mind) in bipolar disorder became an important concern for the researchers.*

*Objectives: evaluation of factors (age of onset, gender, educational level) that influence theory of mind in subjects with Bipolar Disorder.*

*Material and method: a sample of 33 subjects with bipolar disorder was taken into consideration from patients that were hospitalized in the Psychiatry Clinic of Timisoara. We have analyzed the following parameters: socio-demographical (gender, age of onset, educational level), clinical (BPRS score) and theory of mind (Theory of Mind Picture Stories Task). Factors with possible influence in theory of mind were evaluated.*

*Results: the resulted data was compared to literature. The present analysis of ToM ability revealed a deficit in 69,7% of subjects. Also, there is a direct correlation between educational level and theory of mind ( $r = 0,39$ ,  $r$ =correlation ratio).*

*Conclusions: educational level has a direct correlation with the ToM ability, but holds only a reduced influence.*

**Key words:** bipolar disorder, theory of mind, gender, age of onset, educational level

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## INTRODUCTION

The ability of representing, conceptualization and understanding of mental states is one of the greatest achievements of human evolution. The ability to reason mental states has been called Theory of Mind (ToM)(1). Theory of mind in association with attributional style and emotional perception forms a unit called social cognition.

Theory of mind is the central part of social cognition, and also the most analyzed. Many clinical studies have evaluated ToM in Schizophrenia, its manner of influencing social functioning and its relationship to clinical symptoms, educational level and the age of onset. Recently, they have demonstrated that social cognition is different from neurocognition, and that it influences

social functioning in psychotic disorders.

Bipolar disorder associates decreased functioning in social life, profession and family, either during the episodes of illness or in remission periods. This deficit of functioning consists of low social interaction, inability to maintain a job or a steady relationship with a partner. In this case, social cognition (and particularly ToM) plays the main role.

Nowadays there are many ways for explaining ToM, but they are only suppositions. ToM is influenced by many factors: age of onset, clinical symptoms, number of episodes, educational level etc. It is important to analyze these factors for further programs of psychotherapeutic interventions.

## MATERIAL AND METHOD

### 1. Subjects and sample features

Subjects in the current study were recruited from the Psychiatric Clinic of Timisoara, having been hospitalized between 1998-2008, for a first psychotic episode. Due to the decreased number of subjects, the selection was based on inclusion/exclusion criteria, without the use of statistical methods.

#### *Inclusion criteria:*

1. First psychotic episode between 1998 - 2008 that has been hospitalized in the Psychiatric Clinic of Timisoara
2. Current diagnosis - Bipolar Disorder, according to ICD 10 (International Classification of Disorders, World Health Organization) criteria.
3. Out-patients in the Clinical Ambulatory Timisoara
4. All subjects have agreed to participate in the study

#### *Exclusion criteria:*

1. Presence of personality disorders or mental retardation

2. Presence of a illness caused by drugs or an organic disorder

### 2. Assessments

#### 2.1. Clinical symptoms measure

The expanded version of the Brief Psychiatric Rating Scale (BPRS) was used to assess the current level of symptomatology of the subjects. The BPRS contains 24 items, including a wide-range of psychiatric symptoms. The BPRS is rated on a 1 to 7 Likert scale, where 1 indicates no pathology and 7 indicates severe pathology. For this study the BPRS total score for each group was examined.

#### 2.2. ToM evaluation

Theory of Mind Picture Story Task

This test consists of four pictures which create a story, by arranging them in a logical order. Each sequence is pointed (if correct, pictures 1 and 4 are quoted with 2 points, the rest of them with 1 point). There are two questions related to the picture story,

also pointed (1 point for each correct answer). The total score is 8 points, representing “no deficit of ToM”.

#### Theory of Mind Faux-Pas Test

Theory of mind skills were measured using the Faux Pas Task, developed by Baron-Cohen et al.(2). This evaluation consists of 20 vignettes measuring adults’ ability to detect a faux pas. Each story is read for the patient, and then five questions will be asked for each story. These questions include: faux pas detection, identification, comprehension, false beliefs and feelings.

#### 2.3. Analyzed parameters

1. socio-demographic data : gender, age of onset and educational level

2. clinical data: current score of BPRS and number of episodes
3. Theory of Mind(ToM): presence/absence of deficiency of ToM

#### 3. Data analysis

To assess these parameters we have used the existing data about the history of illness, supplemented by a current clinical interview. Subjects were evaluated in the remission period of their illness. Due to the low number of subjects, no statistical data processing was carried out, but only a simple analysis of the results.

## RESULTS

1. Sample characteristics  
Demographic parameters are presented in Table I. The number of subjects was 33, with more than a half

having been female (57,5 %). The average age of onset was of 27.33 years and the average of educational level was of 12.09 years.

Table. I.

Demographic parameters ( N = 33 )

Parameter	%	M (SD)
<b>Gender</b>		
Male	42,5	
Female	57,5	
<b>Age of onset</b>		27,33 (5,29)
<b>Educational level</b>		12,09 (2,73)

N - number of subjects, % - percentage, M - media(average), SD - standard deviation

2. Clinical aspects  
Symptoms level obtained in BPRS were generally in low to moderate range.
3. Theory of mind evaluation  
The application of Theory of Mind Picture Stories Task revealed the following values: 30.3 % of subjects had no deficit in ToM, the rest of 69.7 % presents a range of low to severe deficit.

4. Theory of mind correlation with age of onset, gender and educational level  
Statistical correlation revealed a direct correlation between theory of mind and educational level ( $r=0.3921547$ ,  $r$ -correlation coefficient). Other two parameters, gender and age of onset, have no significant statistical correlation with theory of mind (  $r = 0,08$  for gender and  $r = - 0,14$  for age of onset).



Table. II.

Clinical characteristics (N=33)

Symptoms	M	SD
BPRS Positive	1,54	0,59
BPRS Depression - Anxiety	2,00	0,91
BPRS Negative	1,12	0,32
BPRS Agitation	1,24	0,38
<b>BPRS Total</b>	<b>1,47</b>	<b>0,42</b>

BPRS - Brief Psychiatric Rating Scale, N - number of subjects, M - average, SD - standard deviation

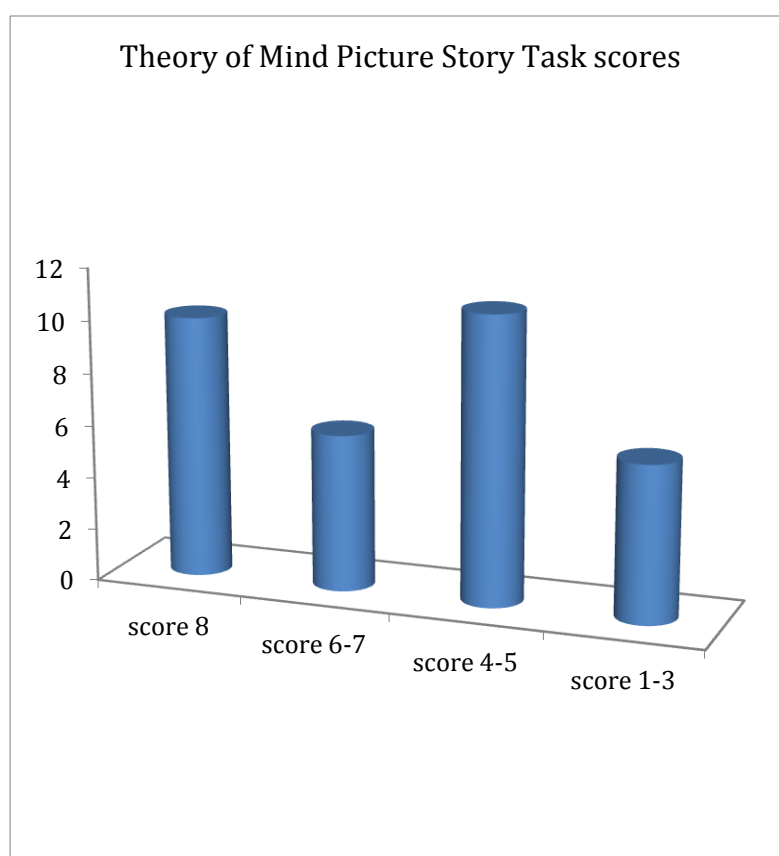


Figure 1. Theory of Mind Picture Story Task scores

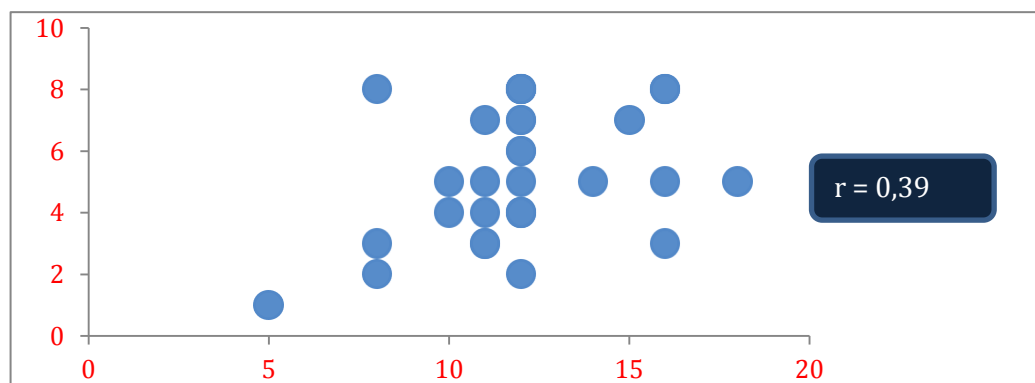


Figure 2. Correlation of educational level and theory of mind (scores of Picture Story Task)

## DISCUSSIONS

The issue presented in this article is part of a study project of social cognition in psychotic disorders. Theory of mind is a central component of social cognition. Most clinical studies have analyzed the relation between theory of mind and clinical symptoms, neurocognition and social functioning.

Most of these studies were on Schizophrenia and its spectrum, and only a low number of them was conducted on Bipolar Disorder. For this paper, we have analyzed the method of how gender, age of onset and educational level can be correlated to theory of mind in subjects with Bipolar Disorder and psychotic elements.

Socio-demographic features revealed that most of the subjects were female, but this has no clinical significance due to the reduced number of subjects in each sample.

The average age of onset is similar to that found in literature. Educational levels are average, which corresponds to Affective Disorders.

BPRS scores showed decreased values, while the subjects were tested in remission. In most of the cases, subjects were in partial clinical remission, maintaining a low intensity of some clinical symptoms.

ToM evaluation revealed that a third of subjects had no deficit. The rest of cases presented a medium (51,5%) or severe (18,2%) deficit. ToM impairment influences social functioning, which is

one of the researched aspect in Bipolar Disorder. Therefore, it is important to analyze the factors that influence ToM: age of onset, gender and educational level.

In literature, the relationship between age of onset and TOM ability has been inconsistent. It is known that as age of onset is even lower, deficit of social cognition is greater, because the age of onset interferes with development of social and cognitive skills(3). The present sample has no correlation between age of onset and ToM abilities( $r = -0,14$ ).

Gender of subjects is another parameter which can influence theory of mind, but in this study no significant statistical correlations were found ( $r = 0,08$ ). In literature there are no studies about the relation of gender and ToM abilities.

Educational level represents an important aspect of ToM research. Clinical studies on Bipolar Disorder revealed a direct correlation between educational level and theory of mind (4). In the present study there is a direct correlation between the two parameters ( $r = 0,39$ ). We can state that as educational level is higher, ToM ability is superior.

The limits of this research are the following:

- low number of subjects ( $n=33$ ) creates no statistical significance
- only the cognitive part of ToM was evaluated, not the emotional one

## CONCLUSIONS

We can affirm that theory of mind has a low influence related to educational level

and almost no influence related to gender of subjects and age of onset.

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# PARTICULARITIES OF SOCIAL COGNITION IN THE DEPRESSIVE-DELUSIONAL PATHOLOGY



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## ABSTRACT

*Social cognition includes the cognitive processes that are used in encoding and decoding the social world. A complete description of social cognition should include the processing of information regarding all the people in our surrounding environment, including ourselves, along with the rules and norms of the social universe. In literature, social cognition is considered to be an important factor in the prediction of the various aspects of social functioning.*

*Aim: to evaluate social cognition in depressive-delusional and delusional-depressive subjects, as well as to perform a comparative analysis according to gender*

*Material and method: for this paper, we have evaluated a sample of 16 subjects diagnosed with depression with psychotic elements (12 women, 4 men) and 27 subjects suffering from paranoid-depressive psychosis (21 women, 4 men), with an evolution of the disorder of over 5 years. The first sample consists of subjects that have a current diagnosis of Recurrent Depressive Disorder and that, along their evolution, have presented at least one episode of Severe Depressive Episode with psychotic symptoms (F33.3, according to WHO ICD-10). The second sample consists of subjects with a diagnosis of Delusional Disorder (F22, according to WHO ICD-10) who have also shown depressive symptoms along their evolution. All subjects have been evaluated in terms of social-demographical and clinical parameters (by using the HAM-D and BPRS rating scales), as well as in terms of social cognition (GEOPTE scale).*

*Results: 62% of subjects show a deficit in social cognition. The comparative analysis shows a more significant cognitive deficit in men (73%).*

*Conclusions: the majority of depressive-delusional patients show a deficit in social cognition, with a more pronounced impairment in male depressive subjects.*

**Key words:** social cognition, depression, delusion

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## INTRODUCTION

Current psychiatric nosology is organized around the idea of spectrum, in order to explain the presence of comorbidities and for the integration of the dimensional perspective with the categorial perspective (1). A maladaptive spectrum is a theoretical construct that is elaborated around a certain categorial disorder and is continued with normality and other nosological categories, similar to the one in view.

For the circumscribing of a spectrum we must also take into account, besides the clinical characteristics of the illness from a longitudinal perspective, the following aspects: subclinical, prodromal, defective aspects, expressed along the lifespan and manifested as an attenuated form of the disorder, characteristics of the underlying personality, the presence of specific or spectrum disorders in first-degree relatives (2).

The depressive-delusional pathology represents an encounter between the affective spectrum (represented in this paper by depression) and the delusional

spectrum, due to the fact that we can discuss about delusional disorders with depressive elements or about depressive disorder with delusional elements (3).

Cognition represents an important element that holds a significant influence on the general functioning of a person. Social cognition represents the ability to recognize, judge and respond accordingly to a certain type of information received from the environment, such as emotions, intentions and the mood of others. Social cognition entails processes that refer to the recognition of social and emotional subtleties represented through facial expression, intonations of the voice, gestures, as well as processes that signify the attribution of mental states of others, empathy and regulation of emotions. The aim of this study was to determine directly the type and level of social and non-social cognitive performance by means of a comparative analysis of two pathologies: depressive-delusional and delusional-depressive.

## MATERIAL AND METHOD

### *Study sample*

Our study sample consisted of 43 subjects (33 women, 10 men) which were divided into two sub-samples: sample A, consisting of 16 subjects with a diagnostic of Recurrent Depressive Disorder (F33, according to WHO ICD-10) and sample B with 27 subjects with a diagnostic of Delusional Disorder (F22, according to WHO ICD-10). All subjects were recruited from the Outpatient Service of the Timis County Emergency Hospital by using inclusion/exclusion criteria. We would like to mention that, due to the reduced number of samples, we have not used any statistical methodology for their inclusion in the study.

### *Inclusion/exclusion criteria:*

- Cathamnesia duration of a minimum of 5 years
- Age of onset under 65 years
- A diagnostic, according to WHO ICD-10, of F22 or F33
- All subjects have agreed to participate in the study
- No history of substance abuse, organic disorder or mental retardation

We have used the SCAN (ICD 10 Structured Clinical Interview) (5) to confirm the clinical diagnostic. The BPRS (Brief Psychiatric Rating Scale) was used to evaluate the current level of clinical symptoms of the subjects. This scale consists of 24 items that

cover a variety of psychiatric symptoms. The BPRS is evaluated on a Likert scale from 1 to 7, where 1 indicates the absence of significant pathology and 7 indicates severe pathology. For this paper, we have examined the total BPRS score for each sample. The HAM-D (Hamilton Depression Rating Scale) was applied for the evaluation of the intensity of the depressive pathology. This scale is one of the most widely used and consists of 21 items, each having a rating from 0-4 according to the severity of the symptom. The total score is interpreted in the following way: 7-17 mild depression, 18-24 moderate depression, and a score of 25 or over indicates severe depression.

The GEOPTE scale is an instrument used for the subjective

perception of the deficit in neurocognition and social cognition. This scale consists of 15 short questions, with answers that range from 1 to 5 on a Likert scale (1 no; 2 little; 3 moderate; 4 enough; 5 very much). The scale should be self-administered by the subjects. Items from 1 to 7 represent questions about basic cognitive functions, while items from 8 to 15 are questions about various aspects of social cognition.

#### *Analyzed parameters*

Socio-demographical: gender, age, onset, instructional level, professional and family status

Clinical: BPRS and HAM-D scores

Social cognition and neurocognition: GEOPTE scores.

## RESULTS

The socio-demographical parameters are presented in table I, comparing the two samples.

Clinical symptoms evaluated by using the BPRS and HAM-D are presented in table II.

The application of the social cognition assessment scale (GEOPTE)

shows the existence of a deficit in both samples and is illustrated in graphic 1. It can be noticed that there are no statistically significant differences between the samples.

Graphic 2 shows the neurocognitive assessment by use of the GEOPTE scale.

Table I

#### Demographic parameters (N=43)

Parameter	% total	% sample A	% sample B
<b>Gender</b>			
Male	23.25	25	22.22
Female	76.74	75	77.77
<b>Age of onset</b>	39.08	39.87	38.29
<b>Educational level</b>	72.10 ss	81.25 ss	62.96 ss
<b>Average duration of evolution</b>	15.44	16.37	14.51

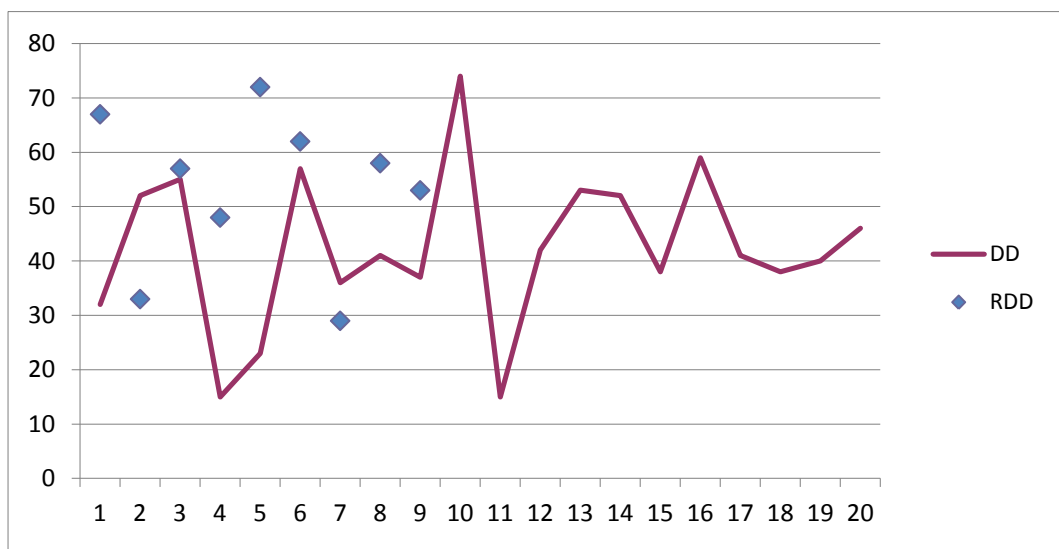
N - number of subjects, % - percentage, ss - secondary school

Table II

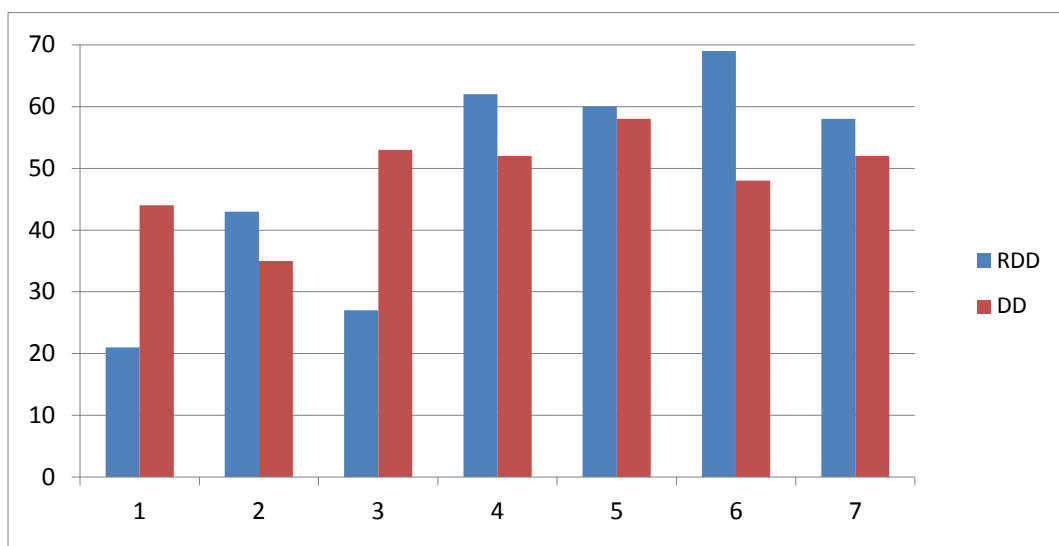
#### Clinical characteristics (N=43)

Assessment scales	M - A	M - B
<b>BPRS Total</b>	<b>26.93</b>	<b>30.74</b>
<b>HAM-D</b>	<b>4.37</b>	<b>3.67</b>

BPRS - Brief Psychiatric Rating Scale, HAM-D - the Hamilton Rating Scale for Depression, N - number of subjects, M- median value, A - sample A, B - sample B



Graphic 1. GEOPTE items for social cognition, a comparison between subjects with Recurrent Depressive Disorder and subjects with Delusional Disorder



Graphic 2. Scores in the GEOPTE items for neurocognition, a comparison between subjects with Recurrent Depressive Disorder and subjects with Delusional Disorder

## DISCUSSIONS

Social cognition represents a very important field when psychoses are involved. For this paper, we have chosen to compare two samples that, theoretically, are part of two different spectra that intertwine.

The evaluation of socio-demographical parameters shows no clinically significant differences between the two samples, this being determined by the low number of subjects. Also, when we compare data from those existing in literature, we

notice that there are many similarities (4).

Regarding the clinical evaluation of subjects, the BPRS scores show much lower values for sample A (depressive-delusional sample) when compared to sample B (the delusional-depressive sample). The low scores can be explained by the fact that all subjects have been evaluated while in the "so-called" remission phase. We would like to mention that all of the subjects included in the study have an incomplete remission with the presence

of a defect. Moreover, all subjects are under maintenance treatment from the first episode to date.

The evaluation of depressive elements was made by using the HAM-D scale and we can notice that the obtained values are relatively low, with the higher score in sample A, compared to sample B.

The GEOPTE scale is used for the appreciation of social cognition, but also for neurocognition. However, this scale is not widely used. It represents an assessment scale that evaluates social cognition in its entirety, without particularizing its components. We have noticed that there were no statistically significant differences between the two samples, an aspect that we have expected to find.

The association between the depressive and the delusional pathology is frequently encountered in psychiatric pathology, bringing about a difficulty when attempting to clinically subsume it in one of the two diagnostic categories, F22 or F33. The delusional theme is the one that could help orientate, but this is also a rather difficult task, especially when we are discussing about paranoid type delusional themes. Depressive elements are important, because the fulfillment of depressive episodes criteria will then orientate us towards F33.

Social cognition is reduced in delusional disorder, but also in

depression, with no comparative clinical studies available in literature. There are only clinical studies that evaluate social cognition for each of these pathologies taken separately. Neurocognition is also reduced in both samples of subjects, this being a predictable aspect, because both diagnostics are in the group of psychoses. It is a well-known fact that in the group of psychoses neurocognition is also affected and that, also, we have to take into account the evolution duration of the illness.

An important issue is the fact that there are currently multiple psychotherapy techniques that could help improve social cognition. This aspect is of great interest because of its consequences on the social functioning of subjects, a functioning that represents one of the most important parameters when evaluating quality of life.

It is also useful to evaluate and intervene on social cognition from the first episode of illness. The earlier the intervention is, the social functioning of subjects will be better, with this aspect being of significance for all of us.

### Limitations

The small number of subjects and lack of homogeneity between samples regarding gender of subjects represent the main limitations of the study..

## CONCLUSIONS

Overall, social cognition is affected in the delusional-depressive pathology, but also in the depressive-delusional pathology, without the possibility of identifying characteristic changes for these pathologies.

More in-depth studies are necessary for each component of social cognition, assuming that they will be able to reveal certain particularities that might be characteristic for each of the studied pathologies.

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# THE IMPACT OF COMPLEX ASSESSMENT ON THE EFFICIENCY OF INCIPIENT OSTEOSCLEROSIS DIAGNOSIS



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## ABSTRACT

*Aim and objectives: The assessment of efficiency regarding the incipient osteosclerosis diagnosis after a complex evaluation.*

*Material and method: 39 patients with hand and knee osteoarthritis underwent digital X-ray evaluation. Each X-ray image was assessed by a doctor and by a software. Osteosclerosis was evaluated in some anatomical regions of the hand and knee. Normal functions of the hand and knee are compulsory in the activities of daily living (ADL).*

*Results: Osteosclerosis was encountered in a high percentage. In only 11.65% of the anatomical regions, there was a contradiction between these 2 evaluations. Osteosclerosis was emphasized in anatomical regions often affected in hand osteoarthritis by using the software, whereas osteosclerosis was denied in regions seldom affected in hand osteoarthritis.*

*Conclusions: A specially developed software can be useful for doctor in view of an early diagnosis and efficient treatment.*

*Key words: osteoarthritis, osteosclerosis software, early diagnosis*

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Arthritis is a disorder with wide etiology, degenerative, inflammatory or infectious. If the etiology is degenerative, the name is osteoarthritis. As a result of life expectancy increase, osteoarthritis has become a public health issue. Hand and knee are often affected in patients with osteoarthritis, these anatomical regions being important in the Activities of Daily Living (ADL). Osteoarthritis has physic impact and psychosocial impact as well. The osteoarthritis treatment relies on the pain and function approaches, as well as on prevention. If an early diagnosis is overlooked, only the pain would be taken into account [1].

The clinical diagnosis is based on the criteria proposed by the American College of Rheumatology. The criteria for hand osteoarthritis are pain or stiffness and 3 out of the following 4: hard tissue enlargement of 2 or more of 10 selected joints, hard tissue enlargement of 2 or more distal interphalangeal joints, less than 3 swollen metacarpophalangeal joints, deformity of at least 1 of 10 selected joints. As for the knee the criteria are knee pain and at least 3 out of the following 6: age over 50 years, stiffness less than 30 minutes, crepitus, bony tenderness, bony enlargement, no palpable warmth [3,4].

Radiology is a useful investigation in reaching a proper diagnostic. This investigation is based on the X-ray properties to be absorbed more or less within the tissues, the bone absorbing more than other tissues. The region within bone, which absorbs more than others, is represented by osteosclerosis. The radiographic criteria for osteoarthritis are: joint-space narrowing, subchondral osteosclerosis, subchondral cyst and osteophytes. Osteosclerosis

stands out as an important sign because it also appears in other serious conditions: metastases and leukemia, osteosarcoma, Ewing's sarcoma, benign tumours, avascular necrosis of the bone, renal osteodystrophy, chronic osteomyelitis, tuberculosis, sarcoidosis, Paget's disease [4].

Nowadays the digital X-ray is frequently used. From a software developer's point of view, a digital X-ray consists of numerical data and semantic data (linguistic values resulting from the conversion of numerical data). In terms of colours, digital X-ray encompasses colorus shades, ranging from black to white. Nevertheless, there is always a problem regarding the vague nature of image (image noise) because of the brightness variation. The digital X-ray processing requires 2 steps. The first one is the image segmentation according to the anatomical regions to be studied. The second step is the extraction of numerical data, followed by their conversion in semantic data and their processing by using the inference based fuzzy system. Inference is defined by the following rule "if variable 1 has ...a linguistic value... variable 2 has ...another linguistic value... then ... conclusion is ...". The linguistic values are deemed as true or false, high or low, gray or white. In the end, a conclusion is written down. Due to the aforementioned rule, false conclusions, as results of brightness variation, are ruled out [5,6].

### **Aim and objectives**

The study aim is the assessment of the efficiency regarding incipient osteosclerosis diagnosis, diagnostic being achieved after a complex evaluation carried out by a doctor and by a special developed software.

39 patients were assessed by a doctor from the Medical Rehabilitation Department. The clinical assessment was carried out according to the criteria provided by the American College of Rheumatology presented above. Afterwards, the patients underwent digital X-ray investigation, the digital X-ray image being assessed by the same doctor. Then a new evaluation of the digital X-ray image was performed, using a special developed software. This software was developed by Norbert Gal, software engineer and assistant professor at The Department of Automation and Applied Informatics of "Polithenica" University of Timișoara.

In the batch of patients, 618 anatomical regions were assessed, 69 metacarpal I bone, 69 proximal phalange of finger 1, 69 phalange groups of fingers (2, 3, 4, and 5), 69 distal extremities of the radial bone, 69 distal extremities of ulna bone, 33 distal extremities of the femur and 33 proximal extremities of tibia.

The digital X-ray images of the aforementioned anatomical regions were assessed by the doctor. Osteosclerosis was assessed by the

doctor as positive, possible or negative. Numerical values were assigned for each evaluation, 2 for positive, 1 for possible and 0 for negative.

Each digital X-ray image was evaluated by the software engineer using the software. The first step was the image segmentation, which was done manually. After the evaluation of the selected regions, a histogram was pointed out. Each histogram corresponds to one of the anatomical regions presented above. As a result of further histogram processing, a numerical value was obtained for each anatomical region ("whiteness"). The average of these numerical values was obtained for each hand ("the hand average whiteness"). For each hand, the numerical value of each anatomical region was compared with the hand average numerical value. This algorithm led to the histogram colour, white or gray. A similar algorithm was carried out for the knee. According to the process performed during the doctor assessment, numerical values were assigned for each evaluation, 2 for positive, 1 for possible and 0 for negative as well.



*Fig. 1 și 2 – Image segmentation*

The next step was the extraction of numerical data from each digital X-ray DICOM file (relative exposure and sensor sensibility). In terms of exposure to X-ray, there were differences between hand and knee exposure. The program evaluated the

hand exposure as correct or overexposed, while the knee exposure was evaluated as correct or underexposed, the evaluation being performed for each anatomical region.

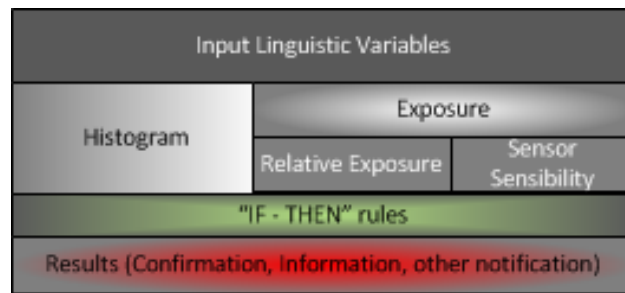


Fig. 3 – The algorithm of the software

In order to write down the conclusions, the fuzzy system based on inference was used. The inference was

based on the “if .... then ....” rule, as shown below.

Table 1 – The assessment performed by the software

Anatomical area	Exposure	Histogram	Osteosclerosis / assigned numerical value
hand + knee	correct	white	positive / 2
knee	underexposed	white	possible / 1
hand	overexposed	white	possible / 1
hand	overexposed	gray	negative / 0
hand + knee	correct	gray	negative / 0

In terms of correlation, the results were obtained by using a graph, Pearson correlation coefficient and regression line. The anatomical regions, where contradiction between the two

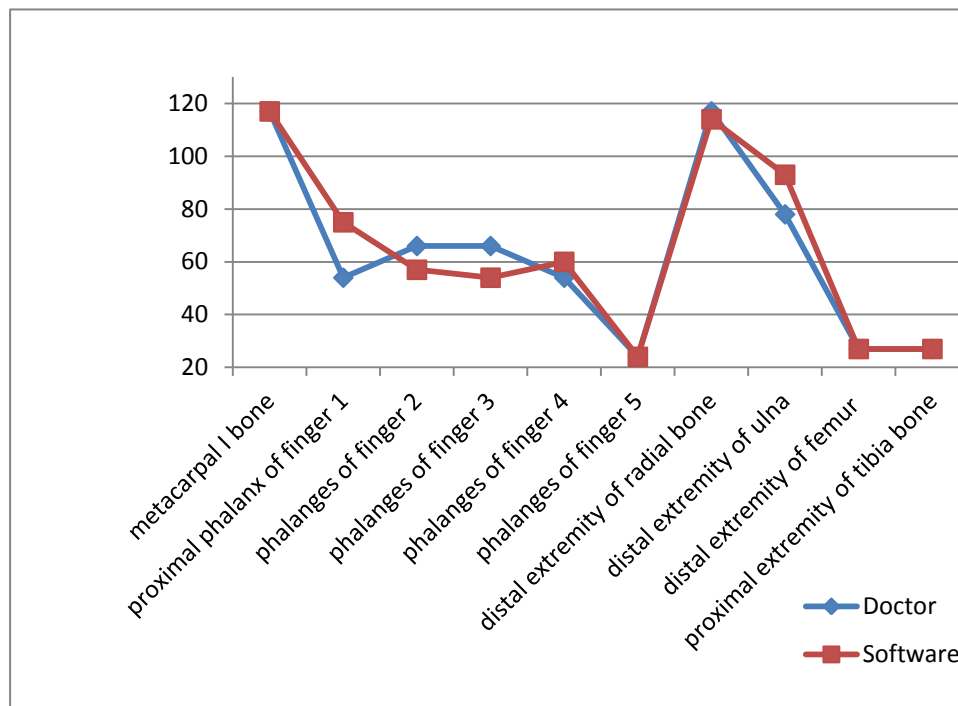
evaluations occurred, were shown before drawing the conclusions. The statistical analysis was carried out by using the Data Analysis function of Microsoft Excel.

## RESULTS

Osteosclerosis was possible and present in 76.92% of the anatomical regions after the doctor’s assessment, this percentage corresponding to 494 anatomical regions. Osteosclerosis was possible and present in 75.25% (465 anatomical regions) after software evaluation.

Differences between the two evaluations were seen only in 72 anatomical areas (11.65%, 1 out of 10

regions). Among these areas, in 45 areas (7.28%) the program emphasized osteosclerosis, these areas being the proximal phalange of finger 1, the phalange group of fingers 2 and 4, as well as the proximal extremity of ulna bone. The possibility of osteosclerosis was infirmed in 27 regions (4.38%), the phalange group of finger 2, the phalange group of fingers 3 and the proximal extremity of the radial bone.



As for the proximal phalange of finger 1, osteosclerosis was shown as present by the software in 30.43% (21 regions out of 69). Osteosclerosis in these 21 regions was deemed as possible by the previous doctor's assessment. After another assessment performed by the doctor, the result of the software was proved to be right. In 21.73% (15 out of 69) of the proximal extremities of ulna bone, osteosclerosis was shown as present by the software, even if the osteosclerosis having been evaluated as possible by the previous doctor's assessment. These 2 aforementioned anatomical regions are especially affected in hand osteoarthritis. Regarding the phalange

group of fingers 2 and 4, osteosclerosis was shown as present by the software in 4.34% (3 out of 39) and 8.68% (6 out of 69). Phalange group of fingers 2 and 4 are seldom affected in hand osteoarthritis.

Nevertheless, osteosclerosis was evaluated as negative in 3 anatomical areas, although osteosclerosis was considered as possible by the previous doctor's assessment. These conclusions were reached in 17.39% of the phalange groups of finger 2 (12 out of 69), in 17.39% of the phalange groups of finger 3 (12 out of 69) and in 4.34% of the proximal extremities of the radial bone (3 out of 69).

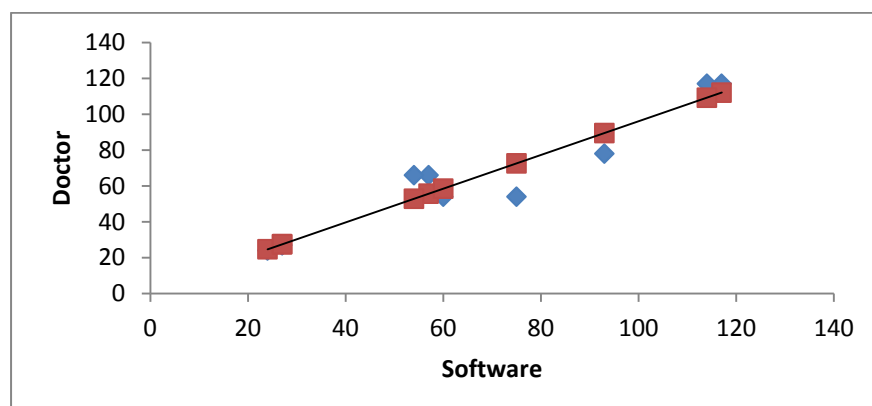


Fig. 5 – The regression line

## DISCUSSIONS

Osteoarthritis is nowadays a most frequently encountered disease. The incipient osteosclerosis is a sign of early osteoarthritis. Osteosclerosis was possible and also present in a high percentage in both evaluations, the results obtained by the software being similar with the results provided by the doctor's assessment. A linear correlation between the two evaluations was seen, the correlation coefficient and the regression line

being proofs of that. Owing to the software, osteosclerosis was confirmed in a higher percentage in regions often affected in hand osteoarthritis, for example in proximal phalange of finger 1 and the proximal extremity of ulna bone. At the same time, osteosclerosis was denied in the phalange group of fingers 2 and 3, these areas being seldom affected in hand osteoarthritis.

## CONCLUSIONS

The aforementioned software turned out to be useful to the doctor. That does not mean that the doctor opinion should be overlooked. The aim of this software is to help the doctor in carrying out of a thorough assessment. Thus, a diagnosis of incipient osteosclerosis and early osteoarthritis can be reached and the proper treatment can be prescribed as soon as possible. An early diagnosis avoids

additional investigations, further irradiations and additional costs. An early diagnosis of hand or knee osteoarthritis is very important because the patient may undergo a proper medical and rehabilitation treatment. Normal functions of the hand and knee joints are mandatory in the activities of daily living (ADL) and for a good quality of life.

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# CHRONIC LUMBOSACRALGIA IN YOUNG ACTIVE ADULTS, A LIFESTYLE RELATED PUBLIC HEALTH PROBLEM?



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## ABSTRACT

*Introduction: Chronic lumbosacralgia, the most frequent musculoskeletal disease, affecting all ages and populational categories, is a public health problem, due to its social implications determined by morbidity and work absenteeism.*

*Aim: Early identification of lifestyle factors with mechanical repercussions on the lumbar spinal column in active young adults, in order to change the management of these diseases, not only medically but also socio-economically.*

*Material and method: For 2 years, between 10.2010-09.2012, 287 young, active subjects, aged between 25-45 years, were clinically, paraclinically and anamnesticly diagnosed with chronic lumbosacralgia in the Western region of Romania and the demographic data and determinant factors of the musculoskeletal sufference were analyzed in order to achieve the proposed objectives.*

*Results: Data analysis showed that of the 287 young, active subjects, identified with chronic lumbosacralgia: 173 were women (60.28%) and 114 men (39.72%), the most affected age group being 35-39 years (32.05%), occupation playing a determinant part in the etiology (50.17% office work); 24.73% overweight and 12.89% obese subjects, 18.11% work >8 hours/day with no or incorrect pauses; 16.37% of the subjects had work incapacity for >21 days during the previous 12 months due to lumbar sufference, and 14.63% were referred to neurosurgical services for an appropriate therapeutic approach. Conclusions: Chronic lumbosacralgia in young, active adults is closely related to lifestyle, and the early identification of determinant factors represents a first stage, of major importance, in the early implementation of an appropriate therapeutic approach and for a successful secondary prophylaxis, with both medical and socio-economic benefits.*

**Key words:** lumbosacralgia, young adult, lifestyle, public health

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## INTRODUCTION

Chronic lumbosacralgia, the most frequent musculoskeletal disorder affecting all ages and populational categories, is a public health problem due to social implications determined by morbidity and absenteeism. (1)

Lumbosacralgia is a frequent cause for health care requests, being extremely expensive and causing considerable loss in productivity, as well as in the capacity to perform daily activities, being considered as a primary disability cause generating costs of 90 billion dollars yearly in the USA. (2)

In the occurrence of lumbosacralgia, static postures contribute together with the muscular imbalance due to weakness of the muscles stabilizing the torso, and the sustained contractions of the spinal extensors during active standing will reduce intervertebral disc nutrition by compression thus increasing the pressure inside the disc. (3)

Pressure in the lumbar intervertebral discs is higher while sitting as compared to standing, the load decreasing while the back is in contact with the lumbar back support of the chair. (4)

During early stages of disc impairment, the patient does not experience pain, at this point the lesion being reversible (5), which is why the early detection of lumbosacralgia associated symptoms is very important, as is the early implementation of appropriate

prophylactic or therapeutic approaches, mainly by correctly informing the population and by a rigorous interdisciplinary collaboration.

Sedentarism and a generalized muscle hypotony, but especially in the abdominal muscles which are involved in stabilizing the spine, are determinant in the occurrence of lumbosacralgia.

On the other hand, mobility loss may lead to early spinal degenerative changes and induces a high risk for further lesions. (6)

### AIM OF THE PAPER

1. Early identification of lifestyle factors (occupation, number of daily working hours, body weight, physical activity), age, gender which have mechanical repercussions on the lumbar spine in young, active adults in order to change the medical and socio-economic management of these diseases;

2. Designing the prophylaxis of the young, active adult who is predisposed to secondary lumbosacralgia of mechanical causes, affecting work capacity, life quality and, last but not least, social life;

3. Elaborating a correct informative programme on occupational chronic lumbosacralgia, its determinant factors, prevention or early treatment options, supported by a rigorous interdisciplinary collaboration.

## MATERIAL AND METHOD

For 2 years, between 10.2010-09.2012, 287 young, active subjects aged between 25-45 years were clinically, paraclinically and anamnesticly diagnosed with lumbosacralgia in the Western region of Romania and demographic data were analyzed together with

determinant factors for musculoskeletal suffering in order to achieve the proposed objectives.

The following parameters were taken into account: age, gender, type of occupation, number of daily working hours, breaks and their duration in occupational or recreative activities,

body weight reported to height, number of workplace absenteeism days during the previous 12 months, thus compiling the profile of the young

active adult predisposed to chronic occupational lumbosacralgia which plays a role in choosing the appropriate therapy or prophylactic plan.

## RESULTS

Data analysis showed that of the 287 young, active subjects identified with chronic lumbosacralgia, women are more frequently affected, the most predisposed occupational category being among office workers (accountants, IT specialists, public officers, teachers, physicians, etc.) and among drivers, while physical workers are less affected, these results being, of course, connected to the modern technologies already implemented in Romania. (Table I, Figures 3,6)

Body weight reported to height in each examined subject is closely related to the occurrence and duration of occupational lumbosacralgia, with 24.73% overweight and 12.89% obese subjects, respectively. (Table I, Figure 4)

Most of the young, active subjects identified with chronic lumbosacralgia work between 4 and 8 hours/day without breaks or taking insufficient or incorrectly spent breaks, and an increased percent (18.11%) work over 8 hours/day which contravenes occupational norms and plays a determinant role in the occurrence of lumbar pathology of mechanical causes. (Table I, Figure 2)

Work absenteeism due to lumbar impairment in young, active adults was significant, with 1:7 subjects being referred to neurosurgery services in order to adopt an appropriate therapeutic approach, due to the severity of the neuro-musculo-arthrokinetic sufference, with further postsurgical recovery therapy. (Table I, Figure 5).

Table I. Risk factors for the occurrence of chronic lumbosacralgia in young, active adults

<b>GENDER</b> (n=287)	60.28 % (n=173) women	39.72% (n= 114) men	-	-
<b>AGE GROUPS</b> (n=287)	16.37% (n=47) 25-29 years	27.17% (n=78) 30-34 years	32.05% (n=92) 35-39 years	24.39% (n=70) 40-45 years
<b>NO. WORKING HOURS</b> (n=287)	14.63% (n=42) <4 hours/day	67.24% (n= 193) 4-8 hours/day	18.11% (n=52) >8 hours/day	-
<b>WEIGHT INDEX</b> (n=287)	62.36% (n=179) normal weight	24.73% (n=71) overweight	12.89% (n=37) obesity	-
<b>DAYS ABSENTEEISM</b> (n=287)	58.53% (n=168) 0-7 days/12 months	14.98% (n=43) 8-14 days/12 months	10.1% (n= 29) 15-21 days/12 months	16.37% (n=47) > 21 days/12 months
<b>OCCUPATION</b> (n=287)	50.17% (n=144) office	30.31% (n=87) drivers	13.93% (n=40) workers	5.57% (n=16) athletes

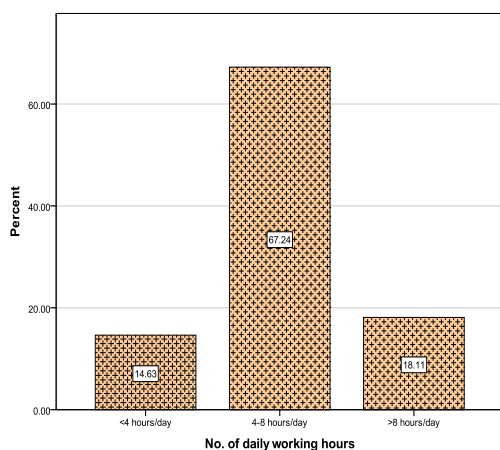


Figure 1. Age groups

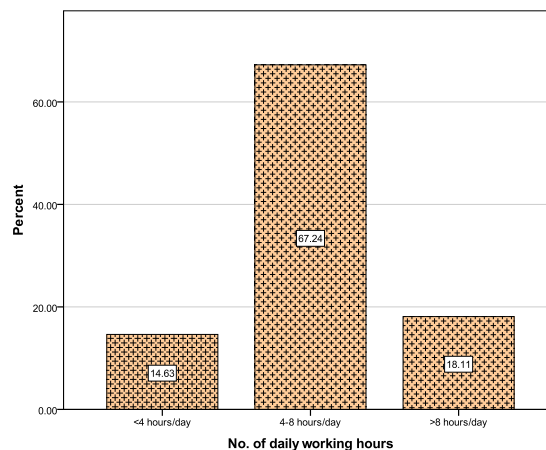


Figure 2. No.working hours/day

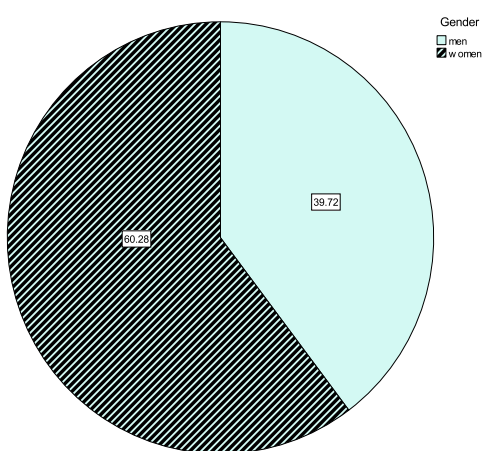


Figure 3. Gender related impairment

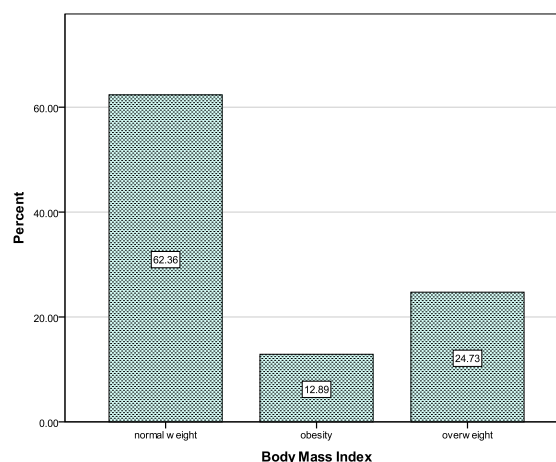


Figure 4. Body weight index

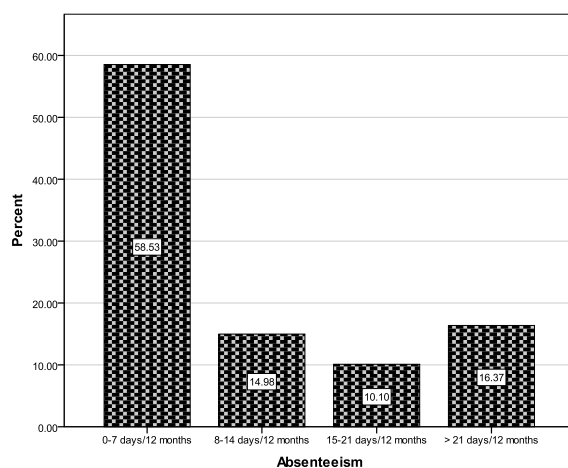


Figure 5. Days of workplace absenteeism/12 months

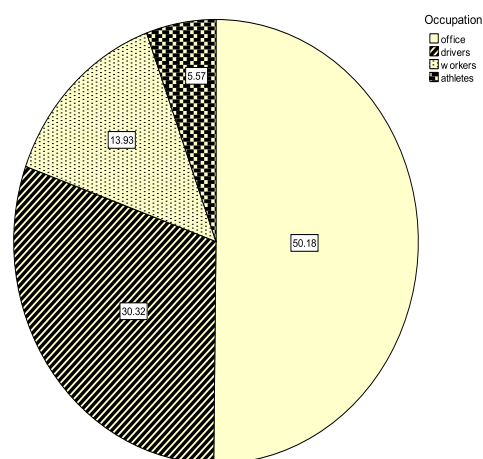


Figure 6. Occupation related chronic lumbosacralgia

## CONCLUSIONS

Chronic lumbosacralgia in young active adults is closely related to lifestyle, and the early detection of

determinant factors represents a first stage of major importance for the timely implementation of adequate

treatment plans and successful secondary prophylaxis, equally achieving medical and socio-economic benefits.

Preventing lumbosacralgia in young active adults is an extremely important aspect for an optimal long-term occupational or recreative activity, with multiple benefits.

Young adults should be made aware of the possible use of ergonomic equipments but also of healthy lifestyles including adequate diets to be constantly followed together with abandoning sedentarism and keeping the body weight within normal limits.

It is imperative for the work programme not to exceed 8 hours/day but short breaks during the work programme are also needed, as a period for back relaxation will decrease fatigue and will lead to adopting a

neutral posture which is very important together with the correct position during the working period and the breaks with stretching elements included.

For the early identification of the symptoms accompanying lumbosacralgia in young, active adults, together with comprehensive clinical, paraclinical and anamnestic examinations, other methods for the early detection of symptoms are imperative by use of non-invasive, last generation equipments such as the ActiGraph which was used in some of the 287 subjects. Repeated assessments are in course and the results and conclusions will be further published, these playing a determinant role in the selection of adequate therapeutic plans with benefits regarding the management of this type of pathology.

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# COMPLICATIONS AND ASSOCIATED PATHOLOGY IN RHEUMATIC INFLAMMATORY DISEASES – A COMPLEX SPECIFIC AND INTERDISCIPLINARY APPROACH



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## ABSTRACT

*Aim and objectives: Determining the frequency and severity of complications and co-morbidities accompanying early diagnosed and therapeutically approached inflammatory rheumatisms and the degree these affect the prognosis of the underlying disease and/or influence the manner in which medication and rehabilitation treatment are conducted.*

*Material and method: A total of 329 patients with early rheumatoid syndrome were evaluated with an early positive diagnosis being formulated in 111 in whom an early staged therapeutic protocol and an interdisciplinary monitoring were introduced for the occurrence of possible complications and/or aggravation of associated pathology.*

*Results: New positive diagnostic criteria together with early targeted therapy allow the decrease in the occurrence rate and intensity of complications and, to a lesser degree, of co-morbidities and, consequently, of the degree these affect the rehabilitation capacity and prognosis, implicitly.*

*Conclusions: An effective multidisciplinary and early approach is needed to investigate and monitor the therapy in these patients according to a certain protocol, data being collected in a standardised file, as well as the training of health care staff members regarding the possible occurrence of complications and aggravation of co-morbidities.*

**Key words:** complications, co-morbidities, interdisciplinary approach, early diagnosis and treatment

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## INTRODUCTION

Rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are autoimmune rheumatic inflammatory diseases severely affecting life quality and with important socio-economic costs due to their long term evolution marked by complications occurring during the activity periods of these diseases, as well as by various co-morbidities (cardiovascular, pulmonary, gastroenterological, metabolic, dermatologic, genitor-urinary, ophthalmologic, etc.) associated to the main disease.

Problems occurring during formulating an early positive diagnosis, as well as the deficiencies in the multidisciplinary approach of these patients, aiming at the identification of already existing or highly probable complications and co-morbidities, in the absence of well structured and coordinated multidisciplinary teams functioning according to clear protocols for the management of these cases and of health care personnel specially trained for correctly

monitoring of patients with the mentioned diseases, may possibly explain the delay in the initiation and/or deficient coordination of therapy and the absence of an appropriate response to treatment in these patients, considering the fact that both associated pathologies as well as complications influence in their turn the prognosis of these patients, increasing, by themselves, the morbidity and mortality rates, as well as the difficulty to obtain an effective therapeutic control of the main disease.

**Aim and objectives.** The study seeks to identify the incidence and stage of complications and co-morbidities in inflammatory rheumatic diseases such as RA, AS and PsA, diagnosed during incipient forms according to new criteria and early approached therapeutically, as well as to determine the degree in which the former affect the capacity to initiate and conduct a medication and rehabilitation treatment and the prognostic of the latter.

## MATERIAL AND METHOD

During the period between January 2010 and June 2012, 329 patients with early non-specific rheumatoid syndrome were evaluated. In order to formulate an early positive diagnosis, the new criteria were used i.e. ACR - EULAR (American College of Rheumatology - European League Against Rheumatism) 2010 for early defined RA [1], and ASAS (Assessment of SpondyloArthritis International Society) 2009 for early AS and PsA, respectively [2,3].

All subjects were early approached therapeutically, benefiting from hygiene, diet and life regimens, orthopaedic hygiene measures, complex rehabilitation treatment, periodically inserted, for 10 days, as

well as medication (symptomatic, DMARD and biologic treatment), individualized and applied according to the stage of the disease and the presence and severity of associated pathology as recommended by present therapeutic protocols.

Patients were monitored for 24 months, with all events (complications and co-morbidities) being recorded from the first day of positive diagnosis up to the completion of the assessment, after two years of complex therapy and interdisciplinary follow up. The most important cardio-circulatory (high blood pressure - HBP, ischemic heart disease - IHD, congestive heart failure - CHF, myocardial infarction - MI, peripheral vascular disease - PVD),

respiratory (asthma, chronic obstructive pulmonary disease - COPD, other respiratory diseases - sleep apnea, interstitial pulmonary fibrosis, pleurisy, etc.), digestive (gastro-duodenal ulcer - GDU, inflammatory bowel disease - IBD and other gastrointestinal diseases, hepatic impairment) complications and/or co-morbidities, as well as the previously mentioned associated autoimmune diseases with hyperlipidemia, obesity (body mass index BMI  $\geq 30$ ), type 2

diabetes mellitus and osteoporosis were included in the statistical analysis.

The statistical data analysis was performed using the MedCalc software, version 12.4.0. Quantitative variables were presented as absolute and percent values comparing RA and AS, RA and PsA and AS and PsA, respectively. Fisher's exact test was used, with p values  $< 0.05$  being considered as statistically significant.

## RESULTS

Of the total number of 329 evaluated patients, early diagnosis according to the new criteria [1,2,3] was formulated in 51 RA (15.50%), 37 AS (11.24%) and 24 PsA (7.9%) cases, with a total number of 111 cases (33.73% of total), including patients of both genders, aged between 17 and 58 years.

After the analysis of cumulated data between the moment of diagnosis and the end of the follow up period, we detected the following absolute and percent values for the frequency of complications/co-morbidities in the monitored group, which, after rounding up to one decimal point, are presented below in figure 1, together with comparisons regarding the frequency of these complications/co-morbidities in the three sub-groups, among the analyzed diseases i.e. RA versus AS, RA versus PsA and SA versus PsA.

In the case of RA, of the total of 51 investigated subjects, the greatest

part had associated HBP (n=15), decreasingly followed by IHD (n=8), hyperlipidemia (n=7), respiratory diseases other than asthma or COPD (n=6), osteoporosis (n=5), equal incidence of asthma and digestive except hepatic diseases (n=4 each), same for MI and type II DM (n=3 each), as well as regarding CHF, PVD, COPD, hepatic impairment and obesity (n=2 each).

Of the 37 AS patients, osteoporosis was the most frequent among the investigated complications/co-morbidities (n=6) followed by HBP, respiratory diseases other than asthma or COPD and digestive other than hepatic diseases, with equal frequency each (n=3), followed by CHF, COPD, hepatic diseases, type II DM and hyperlipidemia (n=2 each), the last place being held by IHD, PVD and asthma (each with n=1). No MI or obesity related events were recorded in these patients..

	x	y	z	p (x-y)	p (x-z)	p (y-z)
<b>Cardio-circulatory system</b>						
High blood pressure	n=15 (29.4 %)	n=3 (8.1 %)	n=7 (29.1 %)	<b>0.0166</b>	1.0000	<b>0.0396</b>
Ischemic heart disease	n=8 (15.7 %)	n=1 (2.7 %)	n=2 (8.3 %)	0.0731	0.4864	0.5558
Congestive heart failure	n=2 (3.9 %)	n=2 (5.4 %)	n=0	1.0000	1.0000	0.5147
Peripheral vascular disease	n=2 (3.9 %)	n=1 (2.7 %)	n=1 (4.1 %)	1.0000	1.0000	1.0000
Myocardial infarction	n=3 (5.9 %)	n=0	n=1 (4.1 %)	0.2605	1.0000	0.3934
<b>Respiratory system</b>						
Asthma	n=4 (7.8 %)	n=1 (2.7 %)	n=2 (8.3 %)	0.3930	1.0000	0.5558
Chronic Obstructive Pulmonary Disease	n=2 (3.9 %)	n=2 (5.4 %)	n=0	1.0000	1.0000	0.5147
Other respiratory diseases (sleep apnea, interstitial pulmonary fibrosis, pleurisy, etc.)	n=6 (11.7 %)	n=3 (8.1 %)	n=1 (4.1 %)	0.7284	0.4185	1.0000
<b>Digestive system</b>						
Gastric ulcer, inflammatory bowel disease, other gastrointestinal diseases	n=4 (7.8 %)	n=3 (8.1 %)	n=1 (4.1 %)	1.0000	1.0000	1.0000
Hepatic impairment	n=2 (3.9 %)	n=2 (5.4 %)	n=1 (4.1 %)	1.0000	1.0000	1.0000
<b>Others</b>						
Osteoporosis	n=5 (9.8 %)	n=6 (16.2 %)	n=2 (8.3 %)	0.5158	1.0000	0.4620
Type 2 diabetes mellitus	n=3 (5.9 %)	n=2 (5.4 %)	n=3 (12.5 %)	1.0000	0.3774	0.3730
Obesity (BMI $\geq$ 30)	n=2 (3.9 %)	n=0	n=5 (20.8 %)	0.5070	<b>0.0309</b>	<b>0.0071</b>
Hyperlipidemia	n=7 (13.7 %)	n=2 (5.4 %)	n=4 (16.6 %)	0.2928	0.7368	0.2000

Figure 1: Absolute (n = number of patients) and adjusted percent values (%) for complications and co-morbidities of RA, AS, PsA obtained in our group of 111 patients, as well as comparisons between proportions expressed as percentage values between RA and AS – p (x-y), RA and PsA – p (x-z) and AS and PsA – p (y-z), respectively. Columns x, y, z represent values found in patients with RA = rheumatoid arthritis, AS = ankylosing spondylitis, PsA = psoriatic arthritis, in the group investigated by our team.

Regarding PsA, of the 24 monitored patients, 7 had HBP, 5 had associated obesity, 4 hyperlipidemia, 3 type II DM, followed by IHD, asthma and osteoporosis (n=2 each), the last place being held by MI, PVD, respiratory diseases other than asthma or COPD, digestive other than liver diseases, all these present in one patient each, with no CHF and COPD cases in this group.

Statistically relevant comparisons (p<0.05), shown with bold characters in the last three columns of figure 1, were recorded between the RA and AS groups and between the AS and PsA groups, respectively, regarding the frequency of associated HBP and between the RA and AS groups and SA and PsA groups, respectively, regarding the incidence of obesity.

## DISCUSSIONS

Percent values indicating the prevalence (incidence) of complications/co-morbidities, show, in some cases, an important decrease in

our group of patients as compared to literature data [4, 5, 6], an illustrative comparison being visible in figure 2, presented below.



	RA(L)	RA	AS(L)	AS	PsA(L)	PsA
<b><i>Cardio-circulatory system</i></b>						
High blood pressure	37.9 %	<b>29.4 %</b>	16.4 %	<b>8.1 %</b>	37.1 %	<b>29.1 %</b>
Ischemic Heart Disease	20.8 %	<b>15.7 %</b>	0.8 %	<b>2.7 %</b>	4.74 %	<b>8.3 %</b>
Congestive heart failure	9.6 %	<b>3.9 %</b>	1.1 %	<b>5.4 %</b>	0.65 %	-
Peripheral vascular disease	5.9 %	<b>3.9 %</b>	0.8 %	<b>2.7 %</b>	-	<b>4.1 %</b>
Myocardial infarction	10.1 %	<b>5.9 %</b>	1.9 %	-	4.74 %	<b>4.1 %</b>
<b><i>Respiratory system</i></b>						
Asthma	8.7 %	<b>7.8 %</b>	3.1 %	<b>2.7 %</b>	8.34 %	<b>8.3 %</b>
Chronic obstructive pulmonary disease	5 %	<b>3.9 %</b>	0.6 %	<b>5.4 %</b>	0.16 %	-
Other respiratory diseases (sleep apnea, interstitial fibrosis, pleurisy, etc.)	11,3 %	<b>11.7 %</b>	0,2 %	<b>8.1 %</b>	2,12 %	<b>4.1 %</b>
<b><i>Digestive system</i></b>						
Ulcer, inflammatory bowel disease, other gastrointestinal diseases	10.3 %	<b>7.8 %</b>	13.9 %	<b>8.1 %</b>	7.2 %	<b>4.1 %</b>
Hepatic impairment	0.1 %	<b>3.9 %</b>	10 %	<b>5.4 %</b>	2.9 %	<b>4.1 %</b>
<b><i>Other</i></b>						
Osteoporosis	15.1 %	<b>9.8 %</b>	-	<b>16.2 %</b>	3.5 %	<b>8.3 %</b>
Type 2 diabetes mellitus	8.5 %	<b>5.9 %</b>	6.2 %	<b>5.4 %</b>	12 %	<b>12.5 %</b>
Obesity (BMI $\geq$ 30)	-	<b>3.9 %</b>	0.2 %	-	30 %	<b>20.8 %</b>
Hyperlipidemia	-	<b>13.7 %</b>	8.6 %	<b>5.4 %</b>	20.7 %	<b>16.6 %</b>

Figure 2 : Comparison between percent values of complications/co-morbidities of arthritis, spondylitis and psoriatic arthritis cited in literature [4, 5, 6] – RA(L), AS(L), PsA(L), and those obtained in our group – RA, AS, PsA

The cumulative incidence of HBP in all the 111 patients decreased with about 8.24% in our group as compared to literature data [4, 5, 6] (from an average of 30.46% to 22.22%), most likely due to the decrease of pain, increase in life quality and improvement of the score of these patients (obtained by targeted and early treatment) and elimination of the pain stress factor. Also, a significant decrease in the frequency of digestive diseases except hepatic ones was found in the entire group of patients and in the frequency of AS associated hepatic diseases, potentially by decreasing the need for early introduction of an aggressive medication (DMARD and/or biologic treatment), with the ability to significantly decrease the unwanted side effects of medication. An important decrease in the incidence of co-morbidities such as type II DM, obesity and hyperlipidemia, was most probably owed to early diagnosis and interdisciplinary approach, before alteration of the patients' general health.

Thus, due to the use of novel criteria allowing an early diagnosis of the main disease, as well as to the timely and targeted clinical-biological

and imagistic investigation of complications/co-morbidities, patients could be approached with adequate therapies diminishing the occurrence rate and severity of complications which characterize inflammatory rheumatic diseases during the stage of constituted disease, as well as those associated to aggressive therapies required for the control of disease activity during the respective stages. Also, there was a decrease in the delayed diagnosis of late stage co-morbidities which could have aggravated by themselves the general medium and long term prognosis of these patients, increasing the effort to control the main disease by medication and rehabilitation treatment.

Even though the analysis and careful data computing allowed a relatively precise assessment, the significant differences as compared to the cited papers are due to the fact that the latter [4, 5, 6] are presented after long term studies (10-15 years), on large groups of patients (sometimes > 10,000 subjects, except the case of PsA), and patient enrolment in these studies was done based upon the old criteria which only allowed a late diagnosis during constituted disease stages [7],

when, due to the delayed introduction of a specific therapeutic protocol and to the lack of timely interdisciplinary investigations, the rapid clinical-biological deterioration and the occurrence of complications and co-morbidities with increasing severity and frequency, influenced the progress and prognosis in these patients, increasing morbidity and mortality rates, as well as the difficulty to establish an effective therapeutic control on the main disease [7]. Even if the genetic factors determining the occurrence of co-morbidities and certain complications could not be controlled, and the influence on triggering factors in the environment was negligible, due to the early diagnosis and the early targeted therapeutic approach and timely interdisciplinary investigation, a good control on disease activity was achieved, also reflected in the low incidence and diminished severity of complications and co-morbidities identified throughout the follow up period.

Our study is the first in Romania to analyze the incidence of complications/co-morbidities of RA,

AS and PsA diagnosed in incipient stages by novel criteria and early approached therapeutically and highlights the differences found in the frequency of these complications/co-morbidities in early diagnosed rheumatic diseases as compared to those found during late stages of constituted disease.

We propose the design of an algorithm to approach the above mentioned patients, whose data will be found in an individual follow up chart for the evolution of the patient, initiated upon the formulation of the positive diagnosis. This chart will include the clinical diagnosis, the stage, the functional diagnosis and the treatment initiated for the main disease, as well as the complications and co-morbidities, presented in detail regarding staging and therapeutic approach, these information being available for the general practitioner, treating specialist, and for all other specialists, and rigorously analyzed and taken into account upon recommending and conducting medication in order to avoid unwanted interactions..

## CONCLUSIONS

In order to significantly reduce the occurrence rate of complications as well as their intensity and unwanted side effects of aggressive medications (needed to control disease symptoms and activity in cases of late diagnosis, frequently associating other pathologies in advanced stages, as well as other complications) and to a lesser extent, the incidence of co-morbidities, an early positive diagnosis, followed by a specific complex therapy are needed together with interdisciplinary collaboration regarding the investigation of any manifestations which might suggest the occurrence of complications or the aggravation of associated co-morbidities, thus decreasing the potential effect on the

rehabilitation capacity and/or prognosis of targeted patients.

Also, it is indispensable to train the health care staff (nurses) regarding the careful monitoring of patients and their therapy, considering that the studied diseases not only affect the muscular and osteoarticular systems, during active disease periods manifestations not directly related to the inflammatory process located in these sites being possible and requiring promptness in reporting to the physician coordinating the complex therapy of these cases, and who is the one abillitated to rapidly refer the patient to the respective specialist and to change the rehabilitation treatment as required..

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# CONSONANTIST PSYCHOSOMATICS CONTRIBUTION OF DOCTOR ȘTEFAN ODOBLEJA TO THE PSYCHOSOMATICS CONCEPT

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## ABSTRACT

*The title Consonantist Psychosomatics is intended to highlight the contribution of Doctor Ștefan Odobleja to the psychosomatics concept which was already underlined in antiquity by Hippocrates.*

*In his work entitled „Consonantist Psychology”, with the aid of nine universal laws, based upon the resonance phenomenon and energetic psychological processes, the creator of generalized cybernetics designs a new model for a psychosomatic approach rendering a cosmic side to the bio-psycho-social model.*

**Key words:** *psychosomatics, consonance, resonance, multidisciplinary, psychological energy, law of reversibility*

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The title is a syntagm composed of two words: psychosomatics and consonantism, these being connected by subordination as well as by correlation of meaning. We may state they may be considered a stable syntactic unit.

From this point of view, the place and role of the great scientist Št.Odobleja in the history of psychosomatics may be established.

Psychosomatics is a medical approach connecting psychological and somatic aspects.

Consonance is defined by Odoobleja as a „physical phenomenon characterized by similitude, selectivity and movement (or vibration) a reversible excitation. A reversibility, a reciprocity, a mutual classification. The identity principle (similitude) and the excluded third party (selectivity) reduced to the physical phenomenon of resonance, a complex phenomenon, caused by sense and frequency similitude with effects of: selectivity, excitation, fusion. The totality of selectivity, amplification, dynamogenics and fusion phenomena produced by superposition of two movements, vibrations similar or related by their direction and frequency” (p.183).

Among the multiple classes of consonance, Odoobleja denominates a physico-psychological and a psychological-physical consonance, i.e. psychosomatic and somatopsychologic.

### BRIEF HISTORY

The psychosomatic unity was underlined as early as Antiquity by Hippocrates, being a concept regarding the human being as a whole, somatic and psychological components being closely interdependent and disease being considered as an individual reaction to the environment.

Anaxagora (504-428 B.C.) was among the first to speak about psychological-somatic dualism (mind-

body relation) which was developed by the great Greek antique philosophers Plato and Aristotle: „the soul gives shape to the body and becomes its vital principle”

The psycho-somatic unity is also found in the Middle Ages in philosophers (XVIIth - XVIIIth centuries) such as Descartes, Hobbes, Berkley, Leibnitz.

The first to talk about psychosomatics in modern times is Heinroth (1818) who was also the one to introduce the term of „somatopsyché” in 1828.

In 1890, Sommer introduces the term of psychogenesis which will be adopted and fundamented by the great creators of psychogenesis theories (P.Janet Freud).

In 1899, Pavlov describes the influence of emotions on physiological processes, conditional reflexes.

In 1912, Adler argued in favour of holism, analyzing the individual rather from the perspective of the entire psychological existence.

In 1922, Deutsch presents the organ nevrosis.

Psychosomatics was introduced as a medical term in the period between 1936-1938 when the first psychosomatic societies emerge and the first specific journals are published.

It is worth mentioning that during the same period, i.e. in the year 1938, the first volume of the French version of consonantist psychology was published in Lugo and distributed through „Librairie Maloine” in Paris and in 1939 the second volume was published, both volumes being distributed to great universities in the world.

We further mention the personalities who contributed to the field of modern psychosomatics: 1943 - Helen Fl. Dunbar with specific personality profiles for each psychosomatic disorder; 1946 - Hans Selye with the general adaptation

syndrome; 1950 - Alexander with conflict specificity; 1957 - Hinkle, Wolff with the determinant role of environmental factors and others such as von Uexkull, Schafer, Sifneos, Batson, Basedovsky, etc.

The encyclopedic dictionary describes Ștefan Odobleja as „...author of the first variant of the generalized cybernetic concept, trying to explain

natural phenomena, and especially those of biology and psychology, by inverse connexion (law of reversibility) notices and highlights the phenomenon of adaptation of living organisms to environmental conditions”, aspect introduced by Hans Selye in 1946. These aspects may be considered a proof of his connection to psychosomatics..

## DISCUSSIONS

As a synthesis, we may state that this concept has passed through several distinct stages in time.

The first Hippocratic stage describes the relation between mind (psyche) and body (soma).

The second stage begins in 1890 with Sommer, who introduces the term of psychogenesis in this relation.

The third stage starts with the modern era when the existential ecological environment is integrated into the psyche-soma unit, i.e. the bio-psycho-social model of Engel - 1974. But in order to establish the starting point of this stage we must go back to the year 1939 when Odobleja, with his work „Consonantist Psychology” and by the law of reversibility (feedback) brings an essential contribution to the psycho-somatic unit by establishing a mutual psycho-somatic relationship. By pluri- and interdisciplinary arguments, he expands the psycho-somatic approach of the human being in the universe. He, thus, creates a novel model, connecting the bio-psycho-social model to the universe by the nine universal laws (equivalence, equilibrium, compensation, reaction, oscillation, inertia, transformation, consonance, reversibility) which he harmonized into a consonance/resonance based upon the law of reversibility and psychological energetical processes for all human life phenomena. He performs an in-depth analysis of the connection between mind, body and universe, rendering a

cosmic side to the model. The psychosomatic approach from a consonantist psychology perspective is demonstrated by Ștefan Odobleja by defining psychological and physical components.

Thus, the physical component is described as the nature, the outside world. „The physical component is the source of psyche and its ultimate expression, cause and, often effect, the fabric of which psyche is made. It is one of the first opposing categories of psyche. From a logical point of view, the physical component is one of the halves of the universe, the other one being the psyche; quantitatively, it is by far the largest part of the universe.” (p. 72).

„The physical component is the exterior, the periphery, the larger sphere; psyche is the inside, the centre, the smaller but the most important portion of each being’s universe.” (p.73).

By describing the physical divisions the author analyzes the physical as the exterior, i.e. the universe but also the human being, with mutual influences between them.

„Psychologically, the physical component is classified as:

- transformable, pre-psyche, excitants;
- transformed, post-psyche, reactions and acts

Biologically, the classification includes:

- the inert nature: the lifeless objects, the physical component per se;
- the living nature: the beings, the biological”.

Further, Odobleja states that the physical component is studied by natural sciences:

- for lifeless nature (cosmological sciences) he describes static sciences (chemistry, geography, mineralogy, astronomy, etc.) and dynamic sciences (physics, mechanics, sky mechanics, etc. - quantum mechanics might be added here)
- for living nature (biological sciences) he similarly describes static sciences (anatomy, histology) and dynamic sciences (physiology, evolution)”(p.73).

Also, the author considers that any psychology must include an introductory study on physics for the following reasons:

1. „The physical always precedes and determines the psyche, thus constituting its cause:

- static causes: - anatomo-histological substrate (the brain); - chemical composition of the substrate
- dynamic causes: - physical excitants; -physiological excitants

2. The physical follows the psyche: it represents its effect, we are thus obliged to study it:

- as a material, static effect: - anatomical, structural; - chemical, constitutional
- as an energetical, dynamic effect: - psychically determined physical phenomena; - determined physiological phenomena.

3. The physical resembles the psyche which confounds with it in several aspects: statically, the psyche may be attributed to a biological structure and to a chemical constitution; dynamically, psychological phenomena are reducible, as a whole, to physical phenomena. (p.74).

Odobleja describes the psyche as being the soul, the spirit, the inner

universe, as a biological function located in the brain. „As any other function, the psyche serves life; it is correlated to each of the other functions of the organism (psycho-physiological correlations). It is strictly dependent to a system of organs. Psychological phenomena are very strictly dependent on circulation and on the physiological status of the organism at a certain moment. Psychological activity is influenced by physical, chemical and biotic agents”(p.p.75, 81). To conclude, Odobleja is the first physician to state that „the true elements of psychological phenomena are invisible - as are the elements or material substrate of physical energies - and analogic, if not identical with the latter. The psychological process is no longer such a rudimentary phenomenon as the presumed mechanical vicinity and removal of neuronic fibers - but an extremely fine, energetic process.”(p.84). This invisible, energetic, vibrational element, intuitively described by Odobleja, is called „string” by some contemporary physicists.

In subchapter on psycho-physiology, the author defines it as a study of „reciprocal repercussions (interreactions) between centre and the periphery, between physical and physiological, between moral and body, between brain and the other viscera, between general and local, between the whole and its parts; the science of psycho-physical reactions. Each organ has relations with all the other organs, including the brain...The brain is, undoubtedly, a privileged organ but it does not hold the monopole on interorganic communications”.(p.425)

He also describes the influences of psyche upon the psychological component, which are: „reversible (functional - in fact, psychosomatic disorders) or irreversible (organic - in fact, psychosomatic diseases); normal (physiological) or abnormal

(pathological); and the influences of the physiological components upon the psyche (somato-psychic action) which also classifies them into reversible and irreversible; normal or pathological, durable or transient”.

Odobleja also mentions that between the physical component and the psyche, between body and soul, there is a mutual influence: each is in its turn cause and effect and he introduces the more accurate notion of reciprocal influence between each body part and each part of the psyche.

We may state that the work of the scientist has open a new perspective for the development of the psychosomatic concept.

In the bibliography studied by Odobleja for his work, which includes 700 papers, we find names of authors cited during the history of psychosomatics such as: Janet P.(1891), Adler (1924), Pieron (1927), Pavlov (1932), Marinescu (1910), Descartes, Freud.

After the “Consonantist Psychology” was published in 1939, in his manuscripts, titles of works on the psychosomatic concept and the atomic universe were found, such as: „Psychosomatic medicine – insights in medical enigmas”, Bonneton Andre, Paris, Librairie Maloine, (1964) and „Man and the atomic universe,” Coudures E, 1951. This demonstrates that he continued to be concerned and studied the way the physical and psychological

components influence one another. Odobleja considers that “the true elements of psychological phenomena are invisible – as are the elements or the material substrate of physical energies – and analogic, if not identical with the latter”.

Nowadays, a lot is said on the psychology of order – quantum psychology (POQP), which is an interdisciplinary synergistic science, built on information from philosophy, psychology, informatics, medicine, physics, biology, cybernetics. POQP seeks the systemic-holistic knowledge of the human psyche universe by means of original measurement instruments and methodologies, based on the generalized quantum theory, in order to optimize human condition from the perspective of the existential purpose and of psycho-somatic and psychological health. Other fields are also mentioned such as quantum medicine, quantum neuroscience and, if all these were to be based on quantum psychology, we might state another syntagm i.e. quantum psychosomatics.

Among the few who mention Stefan Odobleja and his contribution in this area of quantum enigmas, Prof. Ion Mânzat, president of the Romanian Association of Transpersonal Psychology, defines psychological resonance (intuitively described by Stefan Odobleja) as a transpersonal energy vibration explained by expanded psycho-synergy.

## CONCLUSIONS

The main merit of Odobleja is that of intuitively describing the fundamental structure connecting humans to nature (that invisible, energetic, vibration element which physicists describe as “string”. His work radiates a cosmic thinking on life dynamics and is a true resource for ideas in the third millennium.

The value of his work on the psychosomatic concept passed unnoticed during his time. Hopefully, from now on, by our actions, we shall restore the well deserved place in the history of national and international medicine and continue to study his published work and manuscripts kept by the State Archives.



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# COGNITIVE-EMOTIONAL REGULATION STRATEGIES IN RECURRENT DEPRESSIVE DISORDER AND BIPOLAR DISORDER



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## ABSTRACT

*Introduction:* Subjects diagnosed with affective disorders frequently use maladaptive emotion regulation strategies, both in the acute episode and during remission.

*Aim and Objectives:* Assessing the usage frequency of cognitive emotion regulation strategies between RDD and BD patients who are in remission and a control group.

*Material and methods:* 65 patients with RDD, 51 patients with BD and 70 healthy subjects participated in this study. The assessment scales used were: CERQ, HAM-D, YMRS, MINI.

*Results:* Both BD and RDD patients reported using maladaptive coping strategies more frequently and adaptive strategies less frequently when compared to the healthy control group.

*Conclusions:* Assessing cognitive emotion regulation strategies is useful both for assessing the risk of developing a new depressive episode and relapse prevention by promoting the use of adaptive strategies.

**Key words:** emotion regulation, bipolar affective disorder, recurrent depressive disorder, CERQ

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## INTRODUCTION

Emotions are essential survival mechanisms, developed in order to facilitate the avoidance of danger and to promote adaptive behavior (1). Sometimes emotions are triggered virtually automated, other times they appear after a prolonged debate regarding the significance of the event. In both cases, the emotions trigger a coordinated set of tendencies towards a behavioral, experiential and physiological response, which, together, influence our reaction towards a perceived challenge. The emotional response is generated by complex interactions between the limbic neuronal structures (involved in generating and perceiving emotion) and cortical structures (involved in controlling the emotional response), thus generating flexible responses to the external and internal environment (2). Emotional regulation includes any conscious or unconscious process that increases, maintains or decreases one or more aspects of emotion.

Cognitive strategies for emotional regulation are varied. Some are less adaptive and their excessive use may increase vulnerability for psychopathological disorders. Other strategies are adaptive and their use contributes to increased tolerance towards intense emotional experiences, induced by negative and stressful life

events (3). Subjects with recurrent depressive disorder (RDD) and bipolar disorder (BD) have shown a certain inability in modulating emotions in an adaptive manner, both during the acute episode and during remission (4,5). It seems that the habitual tendency to use maladaptive cognitive strategies of emotional regulation reflects well-known neurocognitive deficits (in both disorders), regarding decreased attention control, memory and executive functions (6,7), which have as a substrate abnormalities in the functioning of certain fronto-limbic neuronal networks and their connections, networks which are associated with adaptive emotion regulation (8,9).

### OBJECTIVES

The aim of this study is to assess, using the Cognitive Emotion Regulation Questionnaire (CERQ), the usage frequency of certain cognitive emotion regulation strategies between patients with RDD and BD (who are in remission) and healthy controls. We have also assessed whether there are distinguishable specific cognitive coping strategy profiles for each affective disorder and if some demographical variables influence the tendency to use certain emotional regulation strategies more frequently..

## MATERIAL AND METHOD

Study design was approved by the local ethics committee. The study aim and methods of assessment were explained to all participants prior to the signing of the informed consent.

Three participant groups were selected for this study: 65 patients with RDD, 51 with BD, in remission after a depressive episode and 70 healthy controls matched for age, sex and educational achievement. Both groups of patients were recruited from

psychiatric outpatient facilities in Timisoara. The control group was recruited through collaboration with general practitioners and from non-medical personnel of the Timisoara Psychiatric Clinic. Inclusion criteria for the healthy control group were: signing of the informed consent, no history of psychiatric or severe somatic disorders. Inclusion criteria for the clinical groups were: signing the informed consent, age limit (18-60), diagnoses of either

RDD or BD according to ICD-10 (10) criteria, remission of at least 3 months after a depressive episode (HAM-D score < 5; YMRS score ≤ 2). Exclusion criteria were: refusal to sign the informed consent, other current comorbid psychiatric disorders, the presence of organic or cognitive disorders, current and lifetime substance abuse or dependence.

The present cross-sectional study uses the CERQ questionnaire (Garnesfki, 2002, romanian version) (11) to assess cognitive emotion regulation techniques. The diagnoses of either RDD or BD and the potential current or long-life comorbid disorders were assessed by using the romanian version of the MINI (International Neuropsychiatric Interview, romanian version 5.0.0.) (12). Remission was clinically assessed by the semi-structured interview and verified upon study entry by using the Hamilton Depression Rating Scale (HAM-D) (13) and the Young Mania Rating Scale (YMRS) (14). The following demographical data were assessed: age, sex, educational level. The groups of participants were asked to complete the questionnaire. CERQ is a multi-dimensional questionnaire, which assesses several types of strategies used for emotional regulation triggered by negative or stressful life events. It is comprised of 36 items, grouped into 9 conceptually distinct subscales (4 for each item), which hint toward particular types of emotion regulation strategies. The tendency of a person to engage in each strategy is measured on a 5-point Likert scale (1-almost never –

5-almost always). The subscale score is obtained by adding the individual scores in each strategy, thus, the total subscale score ranges from 4 to 20). The higher the subscale score, the more frequent the cognitive strategy is used. There are four maladaptive and five adaptive subscales. The four maladaptive subscales are as follows: self-blame (blaming one's self for what happened), blaming others (for what happened), rumination (continuous thoughts regarding feelings and ideas associated with the negative event), catastrophizing (increased meaning and terror caused by the event). The five adaptive subscales are: putting into perspective (minimizing the severity of the event by comparing it to other negative events the person has experienced), positive refocusing (distraction from the event by focusing on positive thoughts), positive reappraisal (putting a positive spin on the negative event), acceptance (of the negative event) and refocusing on planning (thoughts on how to manage the negative event). The internal consistency of the values varies from 0.68 to 0.83.

Statistics: Data were processed using IBM SPSS version 18, 2010. For comparison of ordinal and non-parametric data we used the Mann-Whitney test and the Kruskal-Wallis test and for correlation of non-parametric data we used the Kendall test. The level of statistical significance was 0,05, and when Bonferroni correction was applied the level of significance was lowered to 0,025 or to 0,016.

## RESULTS

Regarding demographic data, women were predominant in all three groups. Mean age upon study entry was 43.14 years in the BD group, 46.60 years in the RDD group and 44.30 years in the control group. Disorder duration was significantly higher in the

BD group when compared to the RDD group, as was to be expected ( $U=1051.5$ ,  $z=-3.37$ ,  $p<0.001$ ,  $r=0.31$ ).

Mean values and standard deviation in CERQ subscales for all patient groups are presented in table 1.

Table. 1. Mean subscale values in all participant groups

CERQ subscales		N	Mean	Std. Dev.	Std. Error	95 % confidence interval for mean		Min	Max
						Lower bound	Upper bound		
Self-blame	RDD	65	14.03	2.305	.286	13.46	14.60	10	19
	BD	51	11.73	2.201	.308	11.11	12.34	8	20
	HC	70	9.21	1.605	.192	8.83	9.60	6	13
	Total	186	11.59	2.888	.212	11.17	12.00	6	20
Acceptance	RDD	65	11.62	2.059	.255	11.11	12.13	8	19
	BD	51	11.67	2.046	.287	11.09	12.24	8	15
	HC	70	11.90	2.520	.301	11.30	12.50	7	18
	Total	186	11.74	2.233	.164	11.41	12.06	7	19
Rumination	RDD	65	12.86	4.231	.525	11.81	13.91	6	20
	BD	51	13.12	3.404	.477	12.16	14.07	7	19
	HC	70	11.36	2.007	.240	10.88	11.84	8	17
	Total	186	12.37	3.384	.248	11.88	12.86	6	20
Positive refocusing	RDD	65	11.98	1.709	.212	11.56	12.41	8	15
	BD	51	11.88	2.840	.398	11.08	12.68	8	20
	HC	70	12.17	4.194	.501	11.17	13.17	4	20
	Total	186	12.03	3.125	.229	11.57	12.48	4	20
Refocusing on planning	RDD	65	13.77	1.730	.215	13.34	14.20	11	17
	BD	51	13.78	2.326	.326	13.13	14.44	9	19
	HC	70	14.04	2.493	.298	13.45	14.64	9	20
	Total	186	13.88	2.198	.161	13.56	14.19	9	20
Positive reappraisal	RDD	65	13.98	2.472	.307	13.37	14.60	8	19
	BD	51	9.86	2.173	.304	9.25	10.47	6	16
	HC	70	14.23	3.022	.361	13.51	14.95	9	20
	Total	186	12.95	3.228	.237	12.48	13.41	6	20
Putting into perspective	RDD	65	8.14	2.499	.310	7.52	8.76	4	13
	BD	51	10.24	2.103	.295	9.64	10.83	6	16
	HC	70	13.43	3.100	.371	12.69	14.17	8	20
	Total	186	10.70	3.482	.255	10.20	11.21	4	20
Catastrophizing	RDD	65	14.83	3.343	.415	14.00	15.66	7	20
	BD	51	13.90	3.425	.480	12.94	14.87	7	20
	HC	70	8.06	3.002	.359	7.34	8.77	4	15
	Total	186	12.03	4.482	.329	11.38	12.68	4	20
Blaming others	RDD	65	8.66	2.785	.345	7.97	9.35	4	13
	BD	51	13.31	2.956	.414	12.48	14.15	9	19
	HC	70	7.99	2.887	.345	7.30	8.67	4	17
	Total	186	9.68	3.639	.267	9.16	10.21	4	19

The usage frequency of the nine coping strategies was comparatively assessed in all three patient groups. We found differences regarding the frequency of rating between all three study groups in: self-blame ( $H(2)=101.04$ ,  $p<0.001$ ), rumination ( $H(2)=7.41$ ,  $p<0.05$ ), positive reappraisal ( $H(2)=64.18$ ,  $p<0.001$ ), putting into perspective ( $H(2)=76.88$ ,  $p<0.001$ ), catastrophizing ( $H(2)=89.97$ ,

$p<0.001$ ) and blaming others ( $H(2)=65.32$ ,  $p<0.01$ ). There were no significant statistical differences between the groups of participants regarding the subscales: acceptance, positive refocusing and refocusing on planning ( $p>0.05$ ). Regarding the self-blame subscale, patients with RDD had a higher mean score than BD patients ( $U=767.5$ ,  $z=-4.98$ ,  $p<0.001$ ,  $r=0.46$ ), whilst the mean BD patients score was

significantly higher than that of the healthy subjects ( $U=634.5$ ,  $z=-6.01$ ,  $p<0.001$ ,  $r=0.55$ ).

In the rumination subscale, both patient groups mean scores were significantly higher than that of the healthy control group ( $U=1250.5$ ,  $z=-2.82$ ,  $p<0.01$ ,  $r=0.25$ ). The mean score of the RDD group did not differ significantly from the BD group ( $p>0.05$ ).

In the positive reappraisal subscale, the BD patient group showed significantly lower mean scores than the healthy control group ( $U=459.5$ ,  $z=-6.96$ ,  $p<0.001$ ,  $r=0.63$ ). There were no significant statistical differences between the RDD and BD patient groups ( $p>0.05$ ).

Regarding the catastrophizing subscale, the mean scores of the BD group were significantly higher than the control group ( $U=396$ ,  $z=-7.31$ ,  $p<0.001$ ,  $r=0.66$ ). The mean score of the RDD group did not differ significantly when compared to the BD group ( $p>0.05$ ).

In the blaming others subscale we found higher mean scores in the BD group when compared to the healthy control group ( $U=368.5$ ,  $z=-7.46$ ,  $p<0.001$ ,  $r=0.67$ ). The difference between the mean score of the RDD group and the control group was not statistically significant ( $p>0.05$ ).

We found differences between the two patient groups in the following subscales: self-blame, where the RDD patients had higher mean scores, the blaming others subscale, where BD patients had higher mean scores and the positive reappraisal subscale where BD patients had lower mean scores.

Another aim of this study was to assess whether some demographic data and disorder duration influence the more (or less) frequent use of some cognitive coping strategies in the two patient groups. We found no differences regarding use of strategies of the nine types of cognitive strategies linked to age groups, sex and educational level. We did find differences regarding duration disorder. Thus, RDD patients with a duration disorder of over 10 years, utilized more frequently than those with a disorder duration of under 10 years the self-blame strategy ( $U=339$ ,  $z=-2.09$ ,  $p<0.05$ ) and the acceptance strategy ( $U=337$ ,  $z=-2.13$ ,  $p<0.05$ ). The subgroup of patients with a disorder duration of under 10 years used the putting into perspective strategy more frequently ( $U=329.5$ ,  $z=-2.23$ ,  $p<0.05$ ).

We did not find a differentiated cognitive strategy usage profile in BD patients with disorder duration of less than 10 years or higher than 10 years.

## DISCUSSIONS

In this study we comparatively assessed the usage frequency of cognitive emotion regulation strategies in subjects with RDD and BD in remission after a depressive episodes to a healthy control group. Based on the premise that there will be differences between the groups, we tried to trace if the tendency to use one or another of the nine strategies is influenced by demographical variables and disorder duration. We found distinct performance patterns in the CERQ subscales in both groups of patients when compared to the healthy

controls. Both RDD and BD patients used maladaptive strategies more frequently than adaptive ones, when compared to the healthy controls. These results are in concordance with previous studies, which have assessed this aspect on groups of patients with RDD and BD, during the acute episode and during remission (5, 15). We did not find significant differences between the groups of participants regarding positive refocusing and refocusing on planning, results which contradict results found in older studies (16, 17). In regards to maladaptive strategies,

we found differences between the two patient groups in the self-blame subscale, where RDD patients used this strategy more frequent than those with BD. According to some researchers, this pessimistic attributional style leads to an increase in psychological distress and to its continuity, even in normal subjects, and is considered an important predictor of depression (5). As is rumination, which was frequently rated both by RDD and BD patients in our study. Numerous studies reported that excessive rumination and the negative disposition it maintains increases the risk for the onset of a new depressive episode in both types of affective disorder (18-21). The central mechanism which determines the high and maladaptive level of rumination, both during the acute episode and during remission, is considered to be caused by a dysfunction of attention control (6, 7). In the context of the considerable data gathered until now, which proves the existence of neurocognitive deficits in both affective disorders, it is presumed that dysfunctional cognitive strategies reflect the deterioration of prefrontal executive abilities, abilities which are necessary for assessing the meaning of an event, but also for offering of an alternative perspective and/or an adaptive cognitive-emotional coping strategy (7-9, 22). Adaptive emotion regulation strategies, like the putting into perspective strategy, were significantly less utilized by both patient groups when compared to the healthy controls. Positive reappraisal was used less frequently by BD patients. Taking into consideration that event reappraisal strategies (as a way to regulate emotions) is efficient in the subjective change of disposition, one can conclude that less frequent use of this strategy increases the vulnerability for the subject to develop a depressive episode (23).

Although we found differences between the two patient groups regarding the usage frequency of some

emotion regulation strategies, due to the cross-sectional study design, we cannot interpret them as being specific models for BD or RDD patients, which is in agreement with other studies who found similar cognitive styles in both affective disorders (16, 23). In this study we did not find significant differences between the usage frequency of emotional regulation types used by the participants and the demographical variables studied in the two patient groups. Although we expected that educational level would influence the choice of emotional regulation strategies, our study did not find this differentiation. A possible explanation would be that the usage of certain strategies is mostly determined by the personality structure of the individual as a result of psychosocial and cultural impacts. In comparing the usage frequency of emotional regulation strategies by disorder duration, we found differences only in the RDD group. Thus, in the subgroup with a disorder duration under 10 years, we found significantly higher scores in the putting into perspective subscale, whilst in the subgroup with a disorder duration of over 10 years, we found significantly higher scores in the self-blame and acceptance subscales. The self-blame strategy is considered to be maladaptive and the acceptance strategy is considered to be mixed, having both adaptive features, but also a negative connotation as in a passive resignation, helplessness facing a situation which cannot be altered (24). The fact that there were no differences in BD patients regarding the usage frequency of certain strategies in direct link with disorder duration may be explained by the higher variability of both disposition and cognitive style, bipolar patients being more vulnerable and predisposed to variable kinds of responses to external events as the disorder duration increases (23, 25).

The study has some limitations, and, as such, results are expected to be considered as preliminary. The results

were based on cross-sectional data and it is possible that these could have been under- or overrated. A future, longitudinal study, will allow the assessment of cognitive emotional regulation strategies which persist or change in time. The CERQ questionnaire is of a retrospective self-

assessment type and thus, results may be influenced by context and the memory performance of the assessed subjects. The possible influence of medication and personality traits over the tendency to choose certain emotion regulation strategies was not assessed during this study.

## CONCLUSIONS

The results of this study, with all the aforementioned limitations, support the idea that even during remission, dysfunctional emotional regulation persists, whose expression results mostly by more frequent maladaptive strategy use and less frequent adaptive strategy use by BD and RDD patients, when compared to the healthy control group. The obtained data cannot confirm the existence of typical usage profiles of cognitive emotion regulation strategies in the two patient groups.

Assessing cognitive emotion regulation strategies can be useful from a clinical point of view, both for assessing the risk of developing a new

depressive episode, when the rated scores are high in the maladaptive subscales and for the introduction in the therapeutic plan of psychological interventions, cognitively oriented, which have as an aim the reduction of excessive attempts to control negative emotions or to promote adaptive strategies, thus preventing relapses.

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# PREVALENCE OF DIABETIC RETINOPATHY IN BANAT DISTRICT



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## ABSTRACT

Diabetic retinopathy (DR) is the leading cause of blindness among adults aged 30 to 74 years in the world. DR is causing in addition loss of productivity and quality of life of the patients with diabetes. This fact will lead to additional socioeconomic burdens on the community. However, appropriate treatment can decrease the loss of vision caused by proliferative DR by up to 90%. The purpose of our study was to assess the incidence of diabetic retinopathy among patients from Banat County, Romania who addressed the Ophthalmology Clinic Timisoara. We included in our study the patients who visited the Ophthalmology Clinic Timisoara for eye examination between May 2009 and September 2012. Our study is a retrospective study of 3,400 patients with different eye problems who were examined in Ophthalmology Clinic Timisoara. In all patients with known or recent diabetes a complete physical exam, ECG and blood pressure were performed and afterwards they were referred for a complete eye examination. Required data were collected, including: sex, age, disease duration, type of diabetes, dyslipidemia (based on laboratory findings or use of any lipid-lowering drug). All patients were referred to two ophthalmologists working in our hospital and underwent detailed eye examination. Fundus photography operated with a digital camera and full retinal and macular examination were performed. We found 272 patients (8%) with diabetes. Out of them, 231 patients (85%) had type 2 and 41 patients (15%) had type 1 diabetes. The mean  $\pm$  SD age of the patients included was  $50 \pm 13$  years. The mean follow-up period was  $28 \pm 12$  months. Ophthalmic examination revealed that 109 subjects had some degree of DR (prevalence rate of  $\sim 40\%$ ), including 87 patients with non-proliferative (NPDR) (prevalence rate of 32%), and 22 patients with proliferative diabetic retinopathy (PDR), (prevalence rate of 8%). We detected clinically significant macular oedema (CSME) in 17 patients (6.25%). The incidence of DR was higher in men than in women ( $p < 0.05$ ). We found in our study 49 new patients (18%) with type 2 diabetes. From this patients only five (10%) had DR, four (80%) had NPDR and one patient (20%) had PDR. Among people with insulin treatment the incidence of DR was 70%, 25% in people with oral medication without insulin and 5% in people treated with diet. Diabetic retinopathy has a high incidence in our region among people with type 1 and type 2 diabetes. Most patients have non-proliferative form, but the number of patients with proliferative form is higher than in other studies. In our region the prevalence of diabetic retinopathy is higher in men. Diabetic retinopathy is a public health problem, therefore implication of family physicians, ophthalmologists and diabetologists is mandatory.

**Key words:** Diabetic Retinopathy, Epidemiology, Banat Region

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## INTRODUCTION

Diabetes mellitus (DM) is one of the most common diseases with an increasing incidence worldwide. Recent estimates indicate that there were 171 million people throughout the world living with diabetes in the year 2000, and this number is projected to increase to 366 million by 2030, with the most significant increase occurring in developing countries.[1] Diabetic retinopathy (DR) is the leading cause of blindness among adults aged 30 to 74 years in the world.[2] Vision loss due to diabetic retinopathy occurs through a variety of mechanisms: retinal detachment, preretinal or vitreous haemorrhage, associated neovascular glaucoma, and macular oedema or capillary nonperfusion.[3] DR is causing in addition loss of productivity and quality of life of the patients with

diabetes. This fact will lead to additional socioeconomic burdens on the community.[4] However, appropriate treatment can decrease the loss of vision caused by proliferative DR by up to 90%.[5] Several factors have been identified as determinants for the development of DR and its progression including type and duration of DM, age, glycemic control, hypertension, gender, body mass index (BMI), smoking, serum lipids and presence of microalbuminuria. [6][7][8]

### Purpose

The purpose of our study was to assess the incidence of diabetic retinopathy among patients from Banat County, Romania who addressed the Ophthalmology Clinic Timisoara.

## MATERIAL AND METHOD

**Population.** We included in our study the patients who visited the Ophthalmology Clinic Timisoara for eye examination between May 2009 and September 2012. Our study is a retrospective study of 3,400 patients with different eye problems who were examined in Ophthalmology Clinic Timisoara. Fasting blood samples were taken to assess lipid profile, blood sugar and glycated haemoglobin (HbA1C) levels. We selected for inclusion in our study only patients with fasting plasma glucose of  $\geq 7.0$  mmol/l (126 mg/dl) or more, use of diabetic medications, or a physician's diagnosis of diabetes. We didn't perform oral glucose tolerance testing (2-h plasma glucose  $\geq 11.1$  mmol/l (200 mg/dl)) in the original survey and this item was not included in the case definition. Participants diagnosed with diabetes were categorized as newly diagnosed diabetes (NDM). Those with self-reported diabetes and either on current treatment (insulin or oral

hypoglycaemic medication) or with diabetic glucose values were categorized as having known diabetes (KDM). Type 1 diabetes was assigned to those who started insulin treatment within 2 years of diagnosis. All other cases were classified as type 2. Participants were asked to go to a specified laboratory for collection of blood samples, following a 12-hour fast to identify the undiagnosed patients. Glycosylated haemoglobin (HbA1c) level was measured and values less than 7% considered as indicators of good glycemic control. Body mass index (BMI) (weight in Kg, divided by height in meters squared) was calculated. The WHO (1977, 1979) classification for BMI was used to estimate the degree of obesity.

In all patients with known or recent diabetes was performed a complete physical examine, ECG, blood pressure and was referred for a complete eye examination. Required data were collected, including: sex, age,

disease duration, type of diabetes, dyslipidemia (based on laboratory findings or use of any lipid-lowering drug).

Complete eye examinations were performed. All patients were referred to two ophthalmologists working in our hospital and underwent detailed eye examination. Uncorrected and best corrected visual acuities were determined. The ophthalmologic evaluation included bio-microscope examination of the anterior segment, lens opacity, intraocular pressure measurement and dilated funduscopy. We used the Canon CR6-45NM ophthalmic digital imaging system and Canon EOS 10D digital camera (Canon, Tokyo, Japan) to take 2 digital images

per eye (4 images per participant in total) through a pharmacologically dilated pupil. One image was centred on the macula and the second on the optic nerve. Fundus photography operated with a digital camera and full retinal and macular examination by two experimented operators were performed. Diabetic retinopathy is primarily classified into non proliferative DR (NPDR), formerly termed simple, or background retinopathy (mild, moderate and severe), and proliferative DR (PDR). We use for classification of diabetic retinopathy "The International Clinical Diabetic Retinopathy Disease Severity Scale " (Table 1).

Table 1. International Clinical Diabetic Retinopathy Disease Severity Scale

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**International Clinical Diabetic Retinopathy Disease Severity Scale**

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**Proposed Disease Severity Level**

No apparent retinopathy

**Non proliferative reinopathy**

Mild nonproliferative diabetic retinopathy

Moderate nonproliferative diabetic retinopathy

Severe nonproliferative diabetic retinopathy

**Finding on retinal photography**

No abnormalities

Microaneurysms only

More than just microaneurysms but less than severe NPDR

Any of the following:

More than 20 intraretinal haemorrhages in each of four quadrants

Definite venous beading in two or more quadrants

Prominent IRMA in one or more quadrants

And no signs of proliferative Retinopathy

One or both of the following:

Neovascularization

Vitreous/preretinal haemorrhage

**Proliferative diabetic retinopathy**

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IRMA = intraretinal microvascular abnormalities; NPDR = nonproliferative diabetic retinopathy

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**Statistical Methods**

Statistical analyses were conducted using SAS version 9.2 (SAS Institute,USA) to calculate different values. Characteristics of the study population are described using means for continuous variables and percentages for categorical variables.

For continuous variables, t tests were used and for categorical variables the  $\chi^2$  test. Predictive margins, odds ratios (OR), and 95% confidence intervals (CI) for each were calculated. Associations were considered to be significant if the P value was <0.05.

## RESULTS

We screened 3,400 individuals in our study and we found that 272 (8%) had diabetes. Of them, 231 patients (85%) are with type 2 diabetes and 41 patients (15%) with type 1. The mean  $\pm$

SD age of the patients included was  $50 \pm 13$  years. The mean follow-up period was  $28 \pm 12$  months.

The characteristic of study population is presented in Table 2..

Table 2. Baseline characteristics

	Mean $\pm$ SD
Age	$50 \pm 13$ years
Systolic blood pressure	$128 \pm 9$ mm Hg
Diastolic blood pressure	$82 \pm 9$ mmHg
Men, %	174 pts, 64%
Total cholesterol	$185 \pm 68$ mg%
LDLc	$144 \pm 64$ mg%
Smokers, %	136 pts, 50%
Serum creatinine level	$0.84 \pm 0.12$ mg%
Type 1 diabetes	41 pts, 15%
Type 2 insulin dependent diabetes	68 pts, 25%
noninsulin dependent diabetes	163 pts, 60%

Ophthalmic examination revealed that 109 subjects had some degree of DR (prevalence rate of  $\sim 40\%$ ), including 87 patients with non-proliferative (NPDR) (prevalence rate of 32%), and 22 patients with proliferative diabetic retinopathy (PDR), (prevalence rate of 8%). We detected clinically significant macular oedema (CSME) in 17 patients (6.25%).

Out of the patients with NPDR 41 (15%) had mild form, 32 (12%) moderate NPDR and 14 severe NPDR.

The incidence of DR was higher in men than in women ( $p < 0.005$ ).

We found in our study 49 new patients (18%) with type 2 diabetes. Out of these patients only five (10%) had DR, four (80%) had NPDR and one (20%) had PDR.

Among people with insulin treatment the incidence of DR was 70%, 25% in people with oral medication without insulin and 5% in people treated with diet.

## DISCUSSIONS

The prevalence of type 2 diabetes is between 70 and 90%.[9] In our study we found that 85% (231 patients) of our diabetic patients have type 2 diabetes. Complications of diabetes are macrovascular and microvascular complications. The macrovascular complications include coronary arteries disease, cerebrovascular disease and peripheral vascular disease. The microvascular complications include diabetic nephropathy, diabetic retinopathy, and diabetic neuropathy.

The prevalence of these complications is strongly related to the prevalence, type, and duration of diabetes.

The prevalence of retinopathy at diagnosis of type 1 diabetes is reportedly low, between 0 and 3%.[10][11][12]

Those with newly diagnosed type 2 diabetes have evidence of DR (6.7–30.2%) in several studies. [13][14][15][16] In our study we haven't found any new patients with type 1 diabetes; all the 41 patients (15%)

included are known with type 1 diabetes from several years. The prevalence of new type 2 diabetic patients who were diagnosed in our study was 18% (49 patients).

In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) 1,370 patients given diagnoses of diabetes at age 30 years or older were examined using standard protocols to determine the prevalence and severity of diabetic retinopathy which was found in 50.3% of the patients included. [17]

The prevalence of diabetic retinopathy was examined in people with newly discovered noninsulin-dependent diabetes mellitus ( $n = 50$ ) and in those with previously diagnosed diabetes ( $n = 395$ ) in a population-based study of people aged between 43 and 86 years who lived in Beaver Dam, Wisconsin between 1988 and 1990.[18] Retinopathy was determined by stereoscopic fundus photographs. The prevalence of any retinopathy was 35.2%.

The Rotterdam study included people aged 55 years or older in Holland and reported an incidence of 26% DR among people with diabetes.[19]

In African Caribbean participants in the Barbados Eye Study, who have the same ancestral origin as African Americans, the prevalence of DR in persons with DM was nearly 30.[20]

Among an estimated 10.2 million US adults 40 years and older known to have DM, the estimated crude prevalence rates for retinopathy and vision-threatening retinopathy were 40.3% and 8.2%, respectively.[21]

In the Blue Mountains Eye Study the prevalence of retinopathy was 35.5% based on self-reported diabetes (age range limited to those >49 years with types 1 and 2 diabetes). [22]

The European Diabetes Study (EURODIAB) investigated patients from 31 centres in 16 European countries. The overall mean prevalence of DR in type 1 patients ( $n=3250$ ) for all

the participating centres was found to be 35.9% (range 18.9–68.8%), while the mean prevalence rate for PDR was 10.8% (range 3–19.8%).[23] In the UK, in a population-based study of 10,709 diabetes patients identified through health district audit and data linkage, 16.5% had DR. [24]

The largest Australian study of DR is Newcastle Diabetic Retinopathy Study, a longitudinal study of people of all ages with diabetes conducted over an 11 year period, which reported 35% prevalence of any sign of DR. [25]

We included in our study 272 people aged between 40 and 70 years who live in Banat, a county from Romania. The prevalence of any retinopathy was near 40%, slightly higher than reported in most studies on white population. The most common type of DR in this study was NPDR which was prevalent in 15% (41 patients), data that are similar with other studies mentioned above.. The prevalence of macular oedema in our study (6%) is comparable with the findings obtained from previous reports.

In our study, men had significantly higher prevalence as compared to women. A similar male preponderance has been reported in some studies.[26][27] In contrast, other studies have not shown a consistent pattern of gender variation in DR prevalence.[20][28] In the Singapore Malay Eye Study, a higher prevalence of more severe DR was observed in women; however, this difference was lost after adjustment for metabolic and socioeconomic risk factors.[29] More studies are needed to examine the causes of this inconsistency of DR prevalence in gender differences in different populations. In addition, the present study confirmed the correlations found in other studies between risk factors such as longer duration of diabetes, systemic hypertension and nephropathy and the presence of DR.[30][31]

Our data indicated an association between longer duration of diabetes and increased prevalence of retinopathy. Most of the studies show that the prevalence of DR in type 1 and type 2 diabetes is strongly correlated with the duration of disease. Type 1 and type 2 patients enrolled into the WESDR, which began in 1979 and included 2,990 patients across 11 counties in southern Wisconsin, USA, were more likely to have evidence of DR or PDR the longer the duration of their disease.[32]

There was a significant variation in DR prevalence according to the treatment method used to control diabetes. The prevalence of DR was 70% in patients who used insulin, 25% in patients treated with oral medication without insulin and 5% in those treated with diet. The WESDR also identified an association between insulin treatment and the prevalence of DR or PDR in type 2 patients. Out of the type 2 patients who had evidence of DR, 62% were treated with insulin and 36% were treated without insulin. In a Swedish study where noninsulin-treated type 2 patients were categorized into those treated with oral

hypoglycaemic agents or by diet alone and compared with type 1 patients, DR was identified in a similar proportion of type 1 and type 2 patients treated with insulin (68.3 vs. 65.9%) compared with 30 and 6.7% of type 2 patients treated with oral hypoglycaemic agents or diet, respectively.[33]

A systematic review revealed that tight glycemic control (HbA1c in normal range) reduces the incidence and progression of DR.[34] We didn't study such a correlation in our follow-up.

Our study has some limitation. We included for screening patients who were referred for an eye examination. Moreover, the study included a large representative population, but the results could not be extrapolated to the whole Romania. Our findings clearly demonstrate that DR is a common health problem and may be the leading cause of blindness. The people in our study were aged between 40-65 years, white Caucasian. Thus, caution should be taken when extending these findings to other segments of the population— older and younger age groups, other ethnic groups, etc.

## CONCLUSIONS

The present study was intended to appreciate the incidence of diabetic retinopathy among patients of an Ophthalmology Clinic in Romania. This is very useful in establishing the right treatment for patients because it is well known that diabetic retinopathy is the leading cause of blindness worldwide. Diabetic retinopathy has a high incidence in our region among people with type 1 and type 2 diabetes. Most patients have non-proliferative

form, but the number of patients with proliferative form is higher than in other studies. In our region the prevalence of diabetic retinopathy is higher in men. Appropriate treatment can decrease the loss of vision caused by proliferative DR by up to 90%, therefore accurate diagnosis can save lives. Diabetic retinopathy is a public health problem and implication of family physician, ophthalmologist and diabetologist is mandatory.

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# A CASE OF MANDIBULAR CUNICULATUM CARCINOMA

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## ABSTRACT

*Carcinoma cuniculatum is a rare variant of squamous cell carcinoma. Occurrence in the oro-maxillo-facial region is unusual and was reported in the literature less than 30 times. A 31 year old male presented with pain in the right mandible. X-ray and CT scans showed osteolytic lesions on both jaws. Result of histological study was cuniculatum carcinoma. The tumour is rare entity especially in the head and neck but should be considered as differential diagnosis.*

**Key words:** carcinoma cuniculatum, oro-maxillo-facial, osteolytic lesions

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## INTRODUCTION

Cuniculatum carcinoma is a rare but distinct clinico-pathologic entity, a variety of well differentiated squamous cell carcinoma[1].

The tumour was first described in the foot, although a few cases have also been described involving the oromaxillo-facial region [2]. Involvement of the oral cavity is extremely rare, less than 30 cases are described in literature.

The lesion is a slow-growing proliferation that invades in a burrowing pattern into the surrounding tissues. Metastases to cervical lymph nodes are rare. Local

abscess formation and sequestration are common when the tumour invades bone[3].

Cuniculatum carcinoma is defined histologically by the characteristic infiltrative

pattern of a deep proliferation of stratified squamous epithelium with keratin cores and the absence of any significant cytological atypia which could lead to failure in recognising this tumour as malignant [4].

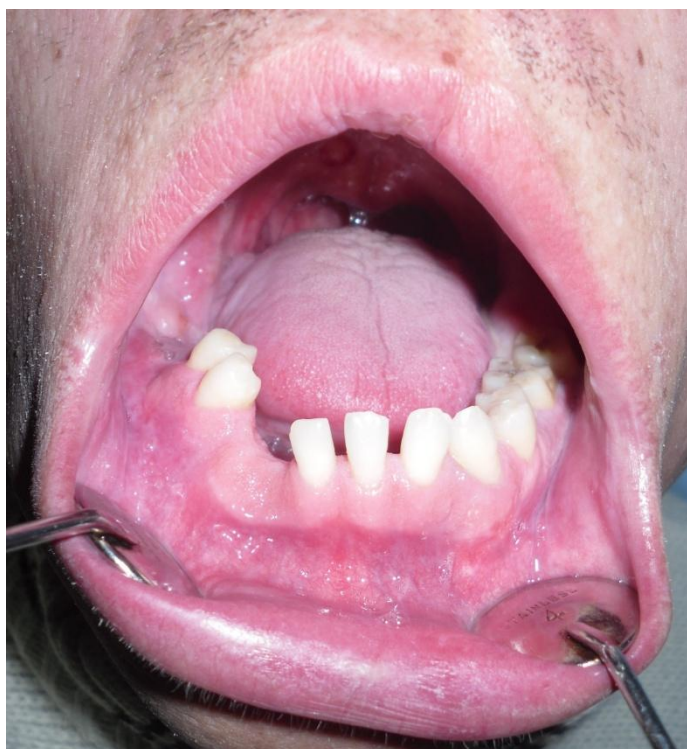
We present a case of cuniculatum carcinoma of the mandibula, the first documented case in the Romanian literature.

## CASE REPORT

Thirty-one years old male presented with progressively increasing swelling on right side of lower jaw for ongoing dental pain in the right lower jaw region over a period of 6 months. The patient was initially treated with antibiotics for a suspected dental abscess (Figure 1).

The panoramic x-ray showed multiple osteolytic lesions in the upper and in the lower jaws (Figure 2).

Plain CT scan showed a lytic lesion involving both rami of the mandible and the maxilla, with ill-defined margins and resorption of the adjacent cortical bone (Figure 3).



*Fig. 1 Clinical aspect of the tumor of the right mandible on physical examination*



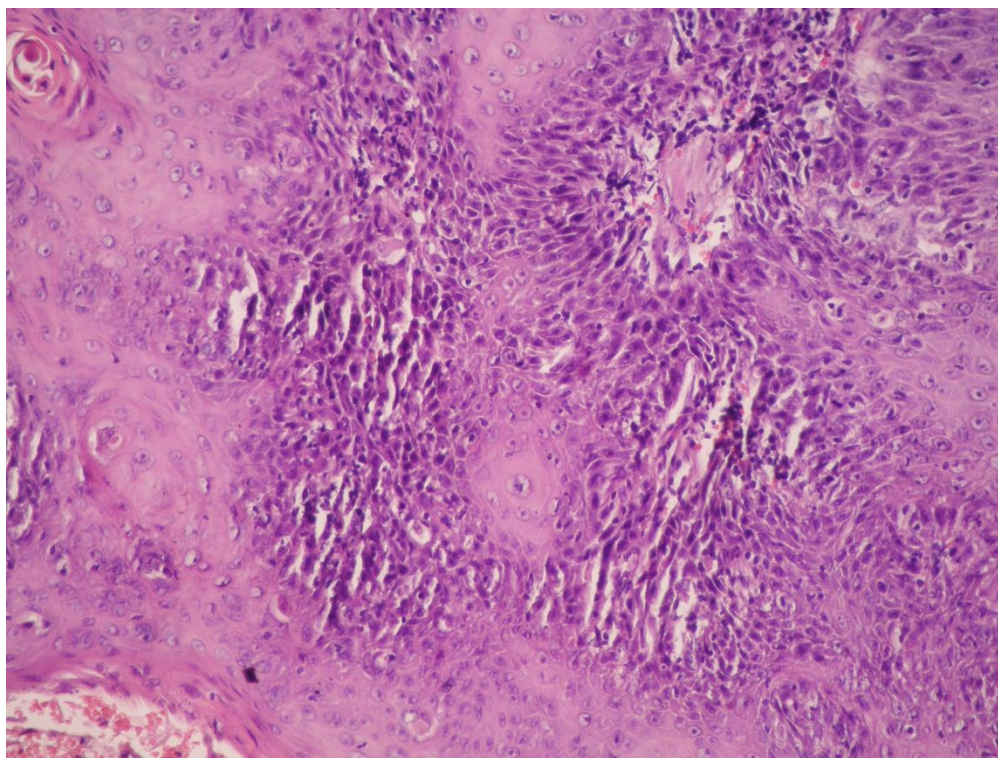
*Fig.2 Panoramic X-ray showed osteolytic change and destruction of the cortical bone*



*Fig.3 Computed tomography scan showed the tumor associated with destruction of the bone in the maxilla and mandible*

Biopsy showed features abnormally proliferating, mildly atypical squamous epithelium	suggesting a well-differentiated squamous cell carcinoma resembling cuniculatum carcinoma (Figure 4).
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*Fig.4 Histologic section (Hematoxylin and eosin 20×) exhibits pathological features of well-differentiated squamous epithelium*

## DISCUSSIONS

Cuniculatum carcinoma is a type of tumour which can affect men, and less frequently women. Studies report higher prevalence rates among men, but methodological differences among the studies make the actual prevalence rate unclear. Our patient was a young man, which is consistent with the masculine tendency noticed for cuniculatum carcinoma in the European literature [5].

Although a number of risk factors have been identified, the causes of carcinoma cuniculatum are not well understood [6]. Alcohol and tobacco have been implicated as aetiological factors in the development of cuniculatum carcinoma of the upper aero-digestive tract [7]; our patients had no history of smoking or alcohol drinking.

The main reason for complaint was pain, symptom most likely caused

by an tumour infection. Clinically, cuniculatum carcinoma appears as an exophytic lesion which mimics a dentoalveolar abscess. Bone involvement is typical in this type of tumor. Is more frequently observed in the maxilla and, in fewer cases, in the mandible, but generally limited to one anatomic site [8]. Our cuniculatum carcinoma case involves both jaws.

Microscopic studies showed a hyperkeratinized tumour with respect to the basal membrane, keratin-filled crypts, and a few cytologic atypies [9].

Although only a small number of cuniculatum carcinoma cases have been described in the literature, studies show recommend wide field surgical resection with good onco-clearance as election therapy because of reported incidence of anaplastic transformation following radiotherapy [10].

## CONCLUSIONS

Cuniculatum carcinoma is a rare entity especially in the head and neck showing local aggressive behavior. Involvement of the oro-maxillo-facial region is extremely rare.

Multiple intraosseous lesions, not affecting the mucosa, were to the knowledge of the author not described before in the literature.

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# CURRENT METHODS FOR IMAGISTIC EVALUATION OF ADULT PATIENTS WITH PERIODONTAL DISEASE UNDERGOING ORTHODONTIC TREATMENT. A REVIEW. PART II: RADIOGRAPHIC EVALUATION.



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## ABSTRACT

*When it comes to assessment of the periodontal bone, radiographic evaluation offers the most reliable investigation at this point. Although the technological advancement in this area of medicine has been significant, still there is a long way to the ideal radiographic evaluation.*

*Part II of this review presents the imagistic solutions available to this day to evaluate the periodontal bone. Both classical methods (periapical radiography, bitewing radiography, panoramic images and subtraction radiography) and modern methods (CT, TACT, CBCT) with all their advantages and disadvantages, quality and reliability, are discussed.*

**Key words:** orthodontics, periodontal treatment, 3d imaging

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According to Armitage diagnosis of periodontal disease is essential to formulate an effective treatment plan which, in turn, affects treatment outcome.[1] A thorough history, clinical examination and radiographic examination are important to establish a periodontal diagnosis. Imaging plays an essential adjunctive role in the diagnostic.[1, 2]

Radiographic examination of periodontal bone is used to assess the degree and pattern of bone loss with respect to the cemento-enamel junction. An ideal radiographic modality to image the periodontium would be one that produces an x-ray beam perpendicular to the image receptor. This would generate an image with the least distortion.[3]

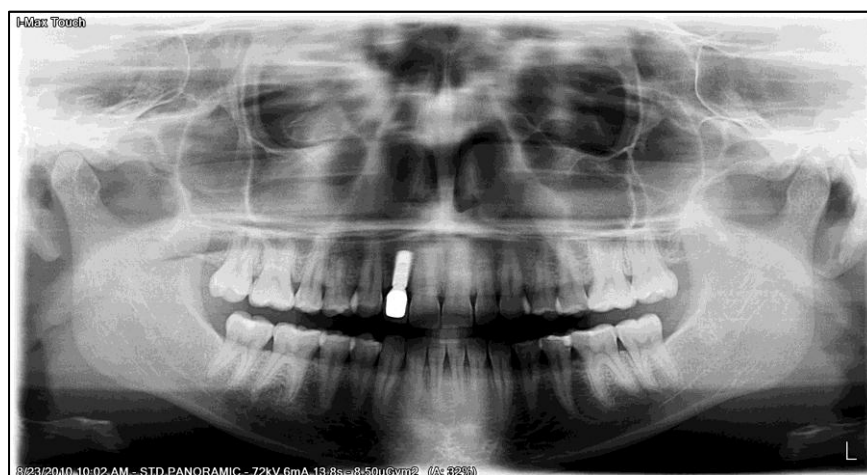
## Classical imagistic evaluation

At present, the classical modalities that best satisfy these requirements are **periapical radiography** and **bitewing radiography**. [4]

Periapical images are used to obtain a clear view of calculus, overhanging restorations, furcation defects and lesions in the apical periodontium.[5] Bitewing radiographs are routinely used to obtain the best view of early interproximal and vertical bone loss.[6]

For the daily common use of both the periodontologist and the orthodontist, **panoramic images** give an overall impression of the maxillary and mandibular dentition and the surrounding alveolar bone. In the daily practice, they serve as screening radiographs and are usually supplemented with periapical films.[7] Moreover, they are the most valuable communication tool with the patient.

However, classical imagistic means may compromise the visualization of alveolar bone due to the limited resolution and blurring of structures of interest.[7] This may be less true for the latest advanced panoramic digital systems (Fig.1). Images obtained from conventional radiographic modalities are in fact two dimensional representations of three dimensional anatomy.[8,9] As a result of the collapse of structures on an image, the view obtained may be unclear, distorted and may suffer from magnification distortions. Linear measurements from conventional radiographs frequently underestimated bone loss compared to clinical probing. Kilic et al. reported that the difference between probing bone loss and radiographic analysis was within one millimeter.[10] Also the correlation between clinical probing and radiographic bone loss decreased as a function of time.



A. Classical panoramic X-Ray





*B. Digital panoramic X-Ray*

*Fig. 1. Quality difference between classical and digital panoramic X-Rays.*

Studies have reported a statistically significant correlation of 0.73 which reduced to 0.07 over a period of one year.[11] Linear measurements have also been attempted on digitized radiographs and on serial radiographs using stored regions of interest in a computer.[12] Though these digital methods reduced the difference in measurement between clinical probing and radiographic bone loss compared to direct measurement on conventional radiographs, the modalities used to obtain these digital images were still two-dimensional and suffered from inherent drawbacks. [10-12]

**Subtraction radiography** is a specialized radiographic technique used to assess periodontal bone loss by comparing serial radiographs.[13] It has been shown that even a 5% change in mineral bone loss can be detected by this technique.[14] In assessing periodontal bone changes, it is essential that the x-ray beam geometry be nearly identical whenever two images are compared.[13,14] Studies have reported various digital methods to produce a nearly identical geometry to compare images, which was difficult to establish earlier.[15] Though the process of obtaining identical geometry for images taken over a period of time improves, the time and effort spent to produce images for use by this technique precludes its clinical use.

### **Modern imagistic evaluation of the periodontal-orthodontic patient**

There is a need for a clear and undistorted view of the periodontal structures to make an accurate diagnosis and evaluate periodontal bone changes over a period of time. This would require the use of a three dimensional modality which would also enable making accurate and reproducible linear measurement of the alveolar bone on a 1:1 ratio.[16-18] Imaging modalities presently available to generate cross sectional images include **Computed Tomography (CT) and Tuned Aperture Computed Tomography (TACT)** .[19]

The routine application of CT for periodontal tissues is currently not indicated, because the risks associated with radiation absorbed dose for the patients do not outweigh the benefits of the information obtained.[20-25] Also, measurements of alveolar bone height in furcation areas from CT images overestimated bone loss by 4 mm or more.[23] Moreover, CT scanners are not available in a dental setting and the cost of obtaining and reformatting a scan is prohibitive. Resolution is also a limiting factor with reformatted CT images.

TACT is an imaging modality situated between transmission radiography and computed tomography.[13, 25, 26] Studies have been done to assess the performance of TACT for various diagnostic

applications, including detection and localization of simulated periodontal defects.[27] The results of these studies showed that TACT enables the isolation of the structure of interest, limited to certain depths in the radiographed volume, by focusing the radiographic information derived from prerecorded projection data. With TACT there is no need to constrain associated projection geometry during the acquisition, which means that stringent patient positioning is not necessary between exposures.[28] The three dimensional images and the number of possible angulation changes that can be made is limited.

A Dental CT technology, Cone Beam CT, is an imagistic tool recently developed, and its applications are being explored in the maxillofacial region.[29-32]

**Cone beam CT(CBCT), Digital Volume Tomography (DVT) or the dental CT**, differ from conventional fan beam CT technique as acquisition process. The x-ray beam is cone-shaped, while that of the conventional CT is fan-shaped (**Fig. 2**). The scanning process in CBCT involves a single rotation of the x-ray source. The image reconstruction process is similar to that of conventional CT. The advantages of cone beam geometry include simplified design and a reduced patient dose. The effective dose from a cone beam scanner is approximately four times greater than that of a panoramic radiograph and 5 to 10 times less than

conventional CT doses.[33-35] CBCT is currently used for pre-surgical assessment of implant sites, orthodontics, and TMJ-related disorders.[29, 30, 36, 37]

In the medical field, the 3D imaging using computed tomography (CT) has been available now for many years, but in the dental specialty, its application is restricted to the use in cases of maxillofacial trauma and diagnosis of head and neck diseases.[38] Routine use of CT in dentistry is not accepted due to its cost, excessive radiation, and general practicality. In recent years, a new technology of cone-beam CT (CBCT) for acquiring 3D images of oral structures is now available to the dental clinics and hospitals. It is cheaper than CT, less bulky and generates low dosages of X-radiations. The innovative CBCT machines designed for head and neck imaging are comparable in size with an orthopantomograph[34].

CBCT provides rapid volumetric image acquisition taken at different points in time that are similar in geometry and contrast, making it possible to evaluate differences occurring in the fourth dimension time. In its various dental applications, images of jaws and teeth can be visualized accurately with excellent resolution, can be restructured three dimensionally, and can be viewed from any angle.[39].

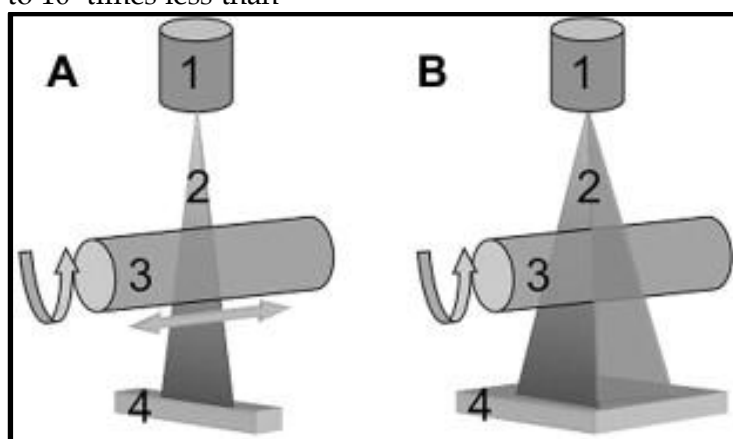


Fig. 2 A Cone beam B CT: (1) X-ray source, (2) beam, (3) rotated object in the course of beam in longitudinal motion (4) line ([www.sciencedirect.com](http://www.sciencedirect.com))

Today, CBCT scanning has become a largely-used imaging modality in periodontology and in implantology, with increasing use in endodontics. For the detection of smallest osseous defects, CBCT can display the image in all its three dimensions by removing the disturbing anatomical structures and making it possible to evaluate each root and surrounding bone. In implant treatment, appropriate site or size can be chosen before placement, and osseointegration can be studied over a period of time [40].

CBCT scanners utilize a two-dimensional detector, which allows for a single rotation of the gantry to generate a scan of the entire region of interest acquiring more than 600 distinct images. The scanning software collects the data and reconstructs it, producing what is termed a digital volume composed of three dimensional voxels of anatomical data that can then be manipulated and visualized with specialized software[36] (Fig. 3) , as compared with conventional CT scanners, whose multiple “slices” must be stacked to obtain a complete image (Fig 4). In comparison with conventional fan-beam or spiral-scan geometries, cone-beam geometry has higher efficiency in X-ray use, inherent quickness in volumetric data acquisition, and potential for reducing the cost of CT.[41] The cone beam technique requires only a single scan to

capture the entire object known as field of view which refers to the area of the anatomy that is captured with a cone of X-rays. Thus, the time required to acquire a single cone-beam projection is the same as that required by a single fan-beam projection.[45]

Although CBCT has existed for over two decades, its true potential has not yet been fully explored, partly because of its high costs. Only recently, it has become possible to develop CBCT clinical systems that are both inexpensive and small enough to be used in operation theaters, medical and dental offices, emergency rooms, and intensive care.

The impact of radiographic imaging on the diagnosis and treatment of periodontal disease has essentially remained unchanged for decades. Fact is that periodontal diagnosis relies primarily on traditional two-dimensional representation of the alveolar bone, with various accuracy degrees. Thus, usefulness of CBCT for periodontal applications is still in progress. Field of interest for the use in periodontology would be the diagnostic and quantitative measurements of soft tissue and alveolar bone levels in three dimensions, imaging of periodontal intrabony defects, dehiscence and fenestration defects, diagnosis of furcation-involved molars, and implant site imaging [24,25,42].



*Fig. 3 Cone Beam CT Digital Volume Rendering*

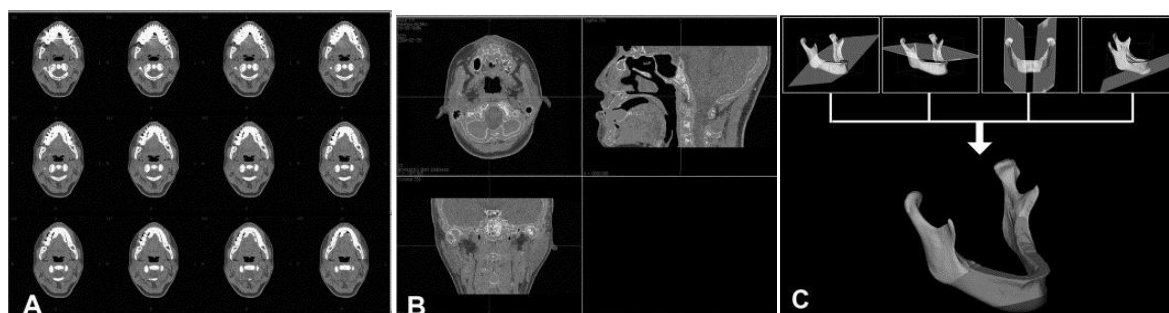


Fig. 4 CT Digital Volume: A 2-dimensional CT images; B, segmentation; C, 3D model rendering

The earliest signs of periodontal disease in radiographs are fuzziness, break in the continuity of lamina dura, and a wedge-shaped radiolucent area at the mesial and distal aspect of the PDL space.[43] In addition to this, the proper observation of PDL space may offer some potential regarding detection of occlusal trauma and the effects of systemic diseases on the periodontium.[44]

When buccal and lingual defects cannot be diagnosed with radiography, CBCT proved to be a superior technique. [47,48] A study on the use of CBCT to examine the geometric relationship between the roots and furcation areas of the mandibular first molars has verified that the X-ray beam projection angle affects the accuracy and diagnosis of a furcation defect. The main reason was that the change in horizontal angulation causes geometric distortion in intraoral radiography.[49]

In the regenerative periodontal therapy, radiographic follow-up of bone healing after grafting is challenging because of the overlapping of gaining and losing areas within the graft. The new volumetric imaging method, CBCT, offers an opportunity to see inside the bone and pinpoint and measure densities in small localized areas such as a vertical periodontal defect, or an alveolar bone graft. This precision would make it possible to reproducibly quantify the bone remodeling after bone grafting. [50]

A recent study showed that CBCT imaging produces images with sub-millimeter isotropic voxel resolution ranging from 0.4 mm to as

low as 0.09 mm.[51] Because of this characteristic, subsequent secondary (axial, coronal and sagittal) and MPR images achieve a level of spatial resolution that is accurate enough for measurement in maxillofacial applications where precision in all dimensions is important such as implant site assessment and orthodontic analysis. Perhaps the most important advantage of CBCT is that it provides unique images demonstrating features in 3D that intraoral, panoramic and cephalometric images cannot.[52] CBCT units reconstruct the projection data to provide inter-relational images in three orthogonal planes (axial, sagittal and coronal). In addition, because reconstruction of CBCT data is performed natively using a personal computer, data can be reoriented such that the patient's anatomic features are realigned.[53] Basic enhancements include zoom or magnification, window/level and the capability to add annotation. Cursor-driven measurement algorithms provide the clinician with an interactive capability for real-time dimensional assessment. Onscreen measurements provide dimensions free from distortion and magnification. Because of the isotropic nature of the volumetric dataset, data sets can be sectioned non-orthogonally, referred to as multiplanar reformation (MPR).[54]

According to Moshiri[53] and Ferrare[54] the **advantages of CBCT** are:

1. It has a rapid scan time as compared with panoramic radiography.

2. It gives complete 3D reconstruction and display from any angle.

3. Its beam collimation enables limitation of X-radiation to the area of interest.

4. Image accuracy produces images with submillimeter isotropic voxel resolution ranging from 0.4 mm to as low as 0.076 mm.

5. Reduced patient radiation dose (29–477  $\mu\text{Sv}$ ) as compared with conventional CT (approx. 2000  $\mu\text{Sv}$ ). Patient radiation dose is five times lower than normal CT, as the exposure time is approximately 18 seconds, that is, one-seventh the amount compared with the conventional medical CT.

6. CBCT units reconstruct the projection data to provide interrelational images in three orthogonal planes (axial, sagittal, and coronal).

7. Multiplanar reformation is possible by sectioning volumetric datasets nonorthogonally.

8. Multiplanar image can be “thickened” by increasing the number of adjacent voxels included in the display, referred to as ray sum.

9. 3D volume rendering is possible by direct or indirect technique.

10. The three positioning beams make patient positioning easy. Scout images enable even more accurate positioning.

11. Reduced image artifacts: CBCT projection geometry, together with fast acquisition time, results in a low level of metal artifact in primary and secondary reconstructions.

Thus, the authors have established the following **indications of CBCT**:

1. Evaluation of the jaw bones which includes the following:

- Pathology;
- Bony and soft tissue lesions;

- Periodontal assessment;
- Endodontic assessment;
- Alveolar ridge resorption;
- Recognition of fractures and structural maxillofacial deformities;
- Assessment of the inferior alveolar nerve before extraction of mandibular third molar impactions;
- Orthodontic evaluation – 3D cephalometry;
- Temporomandibular joint evaluation; and
- Implant placement and evaluation

2. Airway assessment

3. Whenever there is need for 3D reconstructions

In short, CBCT is ideally suited for high-quality and affordable CT scanning of the head and neck in dentomaxillofacial applications [52]

Current CBCT technology has limitations related to the “cone-beam” projection geometry, detector sensitivity, and contrast resolution that produces images that lack the clarity and usefulness of conventional CT images.[55] Another factor that impairs CBCT image quality is image artifact such as streaking, shading, rings and distortion.[56] Streaking and shading artifacts due to high areas of attenuation (such as metallic restorations) and inherent spatial resolution may limit adequate visualization of structures in the dento-alveolar region. [57]

CBCT provides high quality of diagnostic images that have an absorbed dose that is comparable with other dental surveys and less than a conventional CT and thus following the principles of radiation protection to reduce the radiations “as low as reasonably achievable” (ALARA).[34]

## CONCLUSIONS

The need to observe and measure bone and tissue levels evolution during

orthodontic treatment of periodontal patients is vital. The conventional

radiographic investigations such as orthopantomography and bite-wing images offer a fair assessment of the bone offer but sometimes it may be very far from the clinical measurements. Being prone to image distortion caused by the dimensional collapsing of the source (3D to 2D) it would be a mistake to rely entirely on these investigations when an accurate assessment of the bone level is needed.

CT scans have not been designed and developed for specific use in the oral cavity, thus the quality of the received images is many times under the desired needs. Also, the high radiation output for the patient, the cost of the machine and the setup in the

dental practice make it an out of limit option for periodontal assessment.

The only affordable, realistic and reliable imagistic evaluation is the Cone Beam CT. CBCT provides high quality of diagnostic images that have an absorbed dose that is comparable with other dental surveys and less than a conventional CT and thus following the principles of radiation protection to reduce the radiations "as low as reasonably achievable" (ALARA).

To conclude, CBCT with its high spatial resolution, affordability, smaller size, lower acquisition and maintenance have made it the only real choice when it comes to pin-point measurements of bone level during orthodontic treatment..

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# EVALUATION OF THE KNOWLEDGE, SKILLS AND ATTITUDE OF A YOUNG ADULT TOWARDS THE PERIODONTAL DISEASE



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## ABSTRACT

*Periodontal disease is a multi-factorial disease that involves various factors such as: overall health condition, vices, genetic predisposition, and the degree of knowledge and application of dental hygiene. We should not neglect to take into account the social, cultural and geographical issues. Studies on the incidence and prevalence of periodontal disease show a high periodontal disease morbidity in the case of young people aged between 25 and 40 years. For this reason we initiated this study on the assessment of knowledge, skills and attitude of young people towards periodontal disease. Also, we consider that the most effective method that supports both the patient and the clinician is the prevention of periodontal disease. To limit and decrease the incidence of the disease among young people is necessary to establish educational programs which should be applied in parallel with those for the caries-prevention.*

**Key words:** periodontal status, diabetes, tartar, plaque, dental prevention, oral hygiene

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## INTRODUCTION

By the theme chosen for this study we would like to help the specialists that are facing difficulties in diagnosing the conditions in which occurs the periodontal disease, because there are conflicting perceptions of the emergence, evolution and severity of periodontal disease in young adults. Due to the psychological characteristics of a young adult, this age is extremely favorable for the action of oral health education.

Oral health can be defined as an essential part of general health, which allows an individual to speak, eat and live an active social life.

The periodontal diseases are a group of disorders that causes inflammation and destruction of tooth supporting structures. The periodontal disease called "beautiful teeth disease" because it is installed in an area hidden to be seen in a mouth with beautiful

teeth whose shape and position is most agreeable.

The integrity and position of the junction epithelium represents one of the criteria for determining the periodontal status. Any migration in a positive or negative sense of the junction epithelium attachment marks an opening to periodontal disease. For this reason we choose in the questionnaire questions regarding the integrity of the junction epithelium, whose status can be easily notice by everyone with a glance in the mirror.

Many patients come to the dentist after they put themselves the diagnosis of periodontal disease, or when they come to consult and you here them asking: "Do I have periodontitis"? It's a way showing that they are familiar with a concept they know little about. This is why we started this study addressing to the young adults that are still in communities.

## MATERIAL AND METHOD

439 pupil, students and young adults of both sexes, aged between 18 and 40 years were selected. To collect accurate information we tried to achieve their selection to include students in schools and colleges, both in rural and urban environment, and also young people of different social and cultural conditions.

Those who field out a questionnaire were examined in a personal interview and their dento-periodontal status was evaluate in specialized lab.

The questionnaire that we developed included general data (age, sex, school education, living conditions) and knowledge regarding the periodontal disease.

At this interview we added also the dental-periodontal examination in order to correlate the degree of knowledge for some elements: (onset, symptoms, treatment and prevention of periodontal disease) with dental-periodontal disease they have.

The questions had possible answers: yes, no, I don't know.

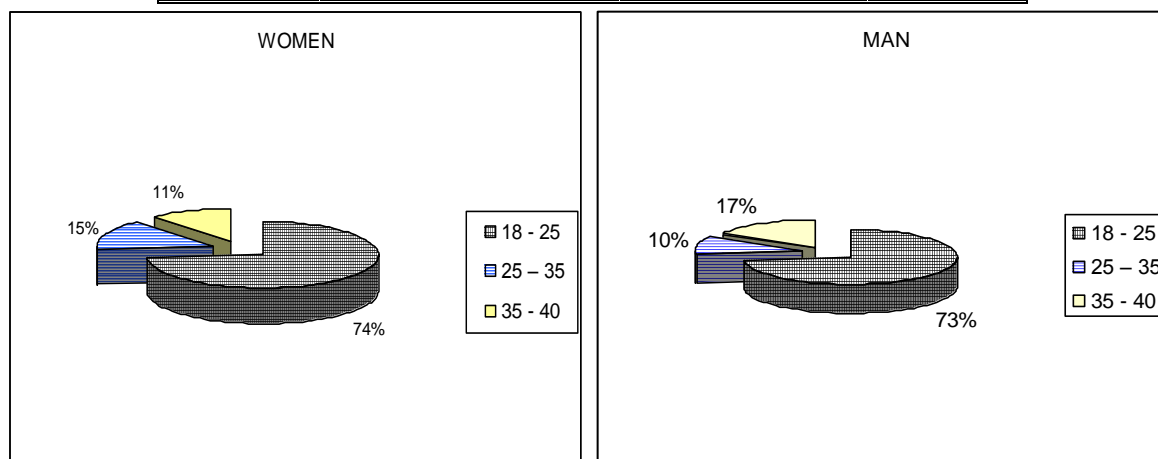
The befits of this type of evaluation are simplicity and the fact it can provide a clear picture of the oral health effects that the one obtained by using a simple dental exam.

Through this it can be done, for example, a clear distinction of age groups.

**Table and graphic no.1**

Distribution of subjects by age and gender

AGE	WOMEN	MEN	TOTAL
18 - 25	169	154	323
25 - 35	34	21	55
35 - 40	26	35	61



It is notice that the numbers of those that were examined is higher in the age group 18 years - 25 years because at this age they are organized in communities (high schools, universities). At the opposite pole are

those with age between 25 years - 35 years - 40 years who are employed and have an active life. For their study we used the dental labs in the localities they live.

**Table no.2****1. Which is the factor that triggers the periodontal disease?****Age group 18 years - 25 years Table no. 2.1**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Tartar	23	7	14	4	5	2
Infection	37	11	27	8	0	0
Malnutrition	8	2	32	10	9	3
Heredity factor	25	8	41	13	4	1
Metabolic disease (diabetes)	14	4	25	8	2	1
Plaque	38	12	18	6	1	0
<b>TOTAL</b>	<b>145</b>	<b>45</b>	<b>157</b>	<b>49</b>	<b>21</b>	<b>7</b>

At this age group analyzing the incidence of positive responses regarding the factor that triggers the periodontal disease the affirmative answers, only 45% show us that their medical education is poor. This fact is fully explained by the lack of oral health education both in schools, and at home. And if at this age the young people are not aware of the factors that trigger the periodontal diseases, by going from their own initiative for control and specialized treatment will conduct to greatly reduce problems.

**Age group 25 years - 35 years Table no. 2.2**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Tartar	8	15	3	5	0	0
Infection	2	4	2	4	2	4
Malnutrition	2	4	6	11	4	7
Heredity factor	5	9	7	13	0	0
Metabolic disease (diabetes)	4	7	4	7	2	4
Plaque	3	5	0	0	1	2
<b>TOTAL</b>	<b>24</b>	<b>44</b>	<b>22</b>	<b>40</b>	<b>9</b>	<b>16</b>

**Age group 35 years – 40 years Table no. 2.3**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Tartar	7	11	2	3	1	2
Infection	1	2	1	2	3	5
Malnutrition	3	5	5	8	3	5
Heredity factor	6	10	8	13	1	2
Metabolic disease (diabetes)	4	7	3	5	3	5
Plaque	5	8	1	2	4	7
<b>TOTAL</b>	<b>26</b>	<b>43</b>	<b>20</b>	<b>33</b>	<b>15</b>	<b>25</b>

This situation is maintained also at the category 25 years – 35 years and also at 35 years – 40 years.

The consequences are relevant regarding the presence of periodontal and gum diseases at this young people.

**Table no.3**

**2. Which is the sign that shows us the onset of the periodontal disease?**

**Group age between 18years – 25 years Table no. 3.1**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Bleeding gums	28	9	34	11	98	30
Gums swelling	9	3	28	9	13	4
Congestive gums	6	2	9	3	24	7
Halitosis	9	3	13	4	10	3
Gums retraction	29	9	10	3	3	1
<b>TOTAL</b>	<b>81</b>	<b>25</b>	<b>94</b>	<b>29</b>	<b>148</b>	<b>46</b>

**Age group 25 years – 35 years Table no. 3.2**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Bleeding gums	14	25	2	4	2	4
Gums swelling	2	4	6	11	3	5
Congestive gums	4	7	8	15	4	7
Halitosis	3	5	1	2	1	2
Gums retraction	1	2	2	4	2	4
<b>TOTAL</b>	<b>24</b>	<b>25</b>	<b>19</b>	<b>45</b>	<b>12</b>	<b>40</b>

**Age group 35 years – 40 years Table no. 3.3**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Bleeding gums	4	7	3	5	7	11
Gums swelling	5	8	4	7	4	7
Congestive gums	2	3	8	13	6	10
Halitosis	2	3	5	8	2	3
Gums retraction	1	2	5	8	3	5
<b>TOTAL</b>	<b>14</b>	<b>23</b>	<b>25</b>	<b>41</b>	<b>22</b>	<b>36</b>

If, for the young people with age between 18 years – 25 years we observe that there where the health education that made the presence, the early signs of the disease are well understood, the subjects over the years do not give the same importance to this signs of onset, the periodontal disease is insidious installing.

**Table no.4**

**3. Which is the measure by which we can combat periodontal disease?**

**Age group 18 years – 25 years Table no. 4.1**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Regular use of paste, tooth brush and floss	94	29	51	16	26	8
Healthy eating	38	12	33	10	26	8
Regular visits to the dentist	30	9	14	4	11	3
<b>TOTAL</b>	<b>162</b>	<b>50</b>	<b>98</b>	<b>30</b>	<b>63</b>	<b>20</b>

50 % of respondents are willing to have a proper oral hygiene by using the paste, tooth brush and floss.

Food consumption was the second important issue. 12% of the young people consider this as the main measure to be taken to combat periodontal disease.

A third problem, sadly 9% detected in terms of prevalence that directly influence the quality of periodontal health, is the regular presence at dental check.

**Age group 25 years – 35 years Table no. 4.2**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Regular use of paste, tooth brush and floss	9	16	1	2	5	9
Healthy eating	4	7	6	11	6	11
Regular visits to the dentist	13	24	7	13	4	7
TOTAL	26	47	14	25	15	27

**Age group 35 years – 40 years Table no. 4.3**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
Regular use of paste, tooth brush and floss	14	23	1	2	6	10
Healthy eating	8	13	4	7	4	7
Regular visits to the dentist	14	23	6	10	4	7
TOTAL	36	59	11	18	14	23

With age increasing, the percentages maintained similar value, which makes me assert that periodontal health education should start as early as possible in schools at the age of young adult.

**Table no. 5**

**4. Can we get rid of breath odor by using mouthwash?**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
TOTAL	201	46	184	42	54	12

Considering that the answers No (43%) and I don't know (12%) in conjunction with periodontal status raises a number of preventive education issues. As prevention is consider more effective the prophylaxis with oral hygiene.

**Table no. 6**

**5. Is there a link between diabetes and periodontal disease?**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
TOTAL	49	11	196	45	194	44

**Table no.7**

**6. Is there a link between diabetes and periodontal disease?**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
TOTAL	72	16	155	35	212	48

The oral cavity may be the site of onset symptoms of internal disease.

Knowing the symptoms, even by the patient, of course it helps us for early detection and therefore for emergency presentation to the dentist, that can change the evolution of the disease, especially its complications and sometimes even the prognosis.

**Table no. 8**

**7. Is there a link between smoking habit and periodontal disease?**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
TOTAL	101	23	214	49	124	28

Even thou smoking is not a determinant factor subsumes other general and local risk factors. From our clinical and radiological observations where it was possible (interalveolar septum lysis), the exposed data confirmed, some of them with an impressive relevance of 49% absence and young people's ignorance for this risk factor. In young adults smoking is an important risk factor in appearance and evolution of chronic and acute periodontal disease. The absence of a sanitary oral education makes for the number of those who gave the answer No or I don't know to be very high.

**Table no.9**

**8. Is there any connection between stress and periodontal disease?**

ANSWER	YES	%	NO	%	I DON'T KNOW	%
TOTAL	57	13	254	58	128	29

Young population (18 years – 25 years) is not influenced by major psychological impact events and their harmful habits are ritualized. A total different situation for the age group (25 years – 40 years) subject to all social and family pressure, which constantly alerts for tomorrow with major responsibilities and well defined affective relations in the family plan. It is the group that has the largest number of cases of periodontal disease, the more exposed are men and in a significant way, the most vulnerable to stress. The preponderance of cases with increased vulnerability to stress and thus to periodontal disease among women in the age group for this segment is due to the efforts related to childbirth and child rearing, but also in the context of profound changes in biological plan. Relevant to this study is that 58% of cases do not consider that periodontal disease onset was due to a strong stress able to disrupt pre-existing mental balance.

## RESULTS

The periodontal health can affect the quality of life regardless the age, mainly through food consumption effects, hygiene of oral cavity, emotional stability and esthetic function. Were identified different causes of these effects, mostly contributing: social-economic and educational situation of the family origin, gingival bleeding, halitosis, dental pathology mobility are the most common signs of periodontal disease that I found.

Periodontal health impact assessment on daily life is relevant to the creation of healthy policies that are addressed to population needs, establishing a priority hierarchy assigned to evaluate the budget treatments.

Providing periodontal services for young people should address not only clinical need, but also focus on socio-dental needs, taking into consideration their perception on the oral conditions impact on every day life.

## DISCUSSIONS

The purpose of this study is to evaluate the knowledge, skills and attitudes of a young adult towards the periodontal disease. In specialized literature this studies regarding the level of knowledge of periodontal health for the young people are not

numerous. Trough this study we tried to draw attention to the low level of knowledge of the periodontal disease signs among young people, especially since in the specialized literature is mentioned an increase in periodontal disease at a young age.

## CONCLUSIONS

The study tries to highlight that exists significant differences in knowledge of onset, the conditions that favor the prevention measures of periodontal disease among people aged 18 and 40, of different social conditions, and educational level.

The observation reflects differences of opinion on the attitudes, behavior and education of the persons examined.

The subjects that come from background with high level, and those that study or come from schools where they participated at oral health education classes, have a better understanding for the causes of periodontal disease, signs of onset, and also periodontal status relations with general health. They are the ones that keep a close relation with the dentist, actively participating at periodic checks.

The observations and data of the research underline the need for implementation oral health education in educational programs in high schools and universities. It is imperative to have sanitary education

of young adults with all available means (practical demonstrations, lectures about hygiene) to obtain a social-hygienic effect that needs to be organized in many and varied actions of oral hygiene.

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# ESTHETICS OF THE SMILE IN ORTHODONTIC TREATMENT

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## ABSTRACT

*Esthetics of the smile is one of the major demands in contemporary orthodontic treatment. In order to improve the smile, it is necessary to analyze the factors that could change aesthetics of the orthodontic patients.*

**Key words:** orthodontic treatment, facial appearance, aesthetic

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## INTRODUCTION

Obtaining a beautiful smile is one of the main aim of any aesthetic dental treatment. In orthodontics, it is not enough only to recognize what is interfering with the smile in order to establish a treatment plan [1].

Teeth aesthetics is not the only parameter that should be measured

when assessing treatment need or treatment outcome [2,3].

The objective of our present study was to evaluate whether dental aesthetics correlates with facial apperance.

## MATERIAL AND METHOD

From the records of the Department of Orthodontics, University „Carol Davila“ of Bucharest, patients of two different age groups were chosen.

Two groups of patients were used in this study, prior to and on completion of orthodontic treatment: first group consisted in 20 patients (10 males and 10 females), that were 12-15 years of age and were in the pre-ortodhontic treatment stage. The second group is represented by a number of other twenty patients (10

males and 10 females), of the same age, that were in the post-treatment stage.

These follow-up was three years for both groups.

Facial and oral photographs were used for evaluation. Facial apperance was determined at two different ages on the facial photographs (Figure 1).

Scoring of dental apperance was carried out using is scored by a standardized series of photographs (Figure 2).



*Fig. 1 Facial photographs before and after orthodontic treatment*





*Fig. 2 Oral photographs before and after orthodontic treatment*

## RESULTS

After grouping the sample according to sex and orthodontic treatment stage, we established that in the pre-treatment phase the facial appearances for male patients showed significant correlation with dental appearance ( $P < 0.05$ ).

In the post-treatment group of the same age, a similar correlation was found among female patients.

For the second group of both sexes, significant correlations were found between facial and dental appearances.

No significant correlations existed between the increments of facial appearance and the increments of dental appearance.

## DISCUSSIONS

Facial and dental appereances of both groups were assessed with two different methods.

In our sample, dental and facial appereances were significantly correlated only in male patients at the pre-orthodontic treatment stage.

Besides it is known that male patients seeking orthodontic treatment have more severe anomalies than females [4].

Our study shows that facial appereance improved in the group of

patients undergoing orthodontic treatment during the follow-up.

Facial and dental appereances did not significantly increase in the group that was already in the who did not undergo active treatment during the follow-up; therefore, the changes after treatment were negligible.

These data support the fact that both facial and dental appereance could be affected by various factors [5,6].

## CONCLUSIONS

Evaluation of the factors that could change aesthetics gives a higher

possibility of success in the treatments that include such objectives.

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# OBSERVATIONS ON THE IMPACTED MAXILLARY CANINE

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## ABSTRACT

*This article reports the complication rate for surgical-orthodontic procedures for impacted upper canine. Thus, 20 consecutively treated patients with palatally impacted upper canines were examined. For ten cases the ectopic tooth was surgically exposed alone and for the other ten patients an orthodontic bracket was intraoperative bonded. The long-term outcome of the teeth which have been exposed in these two ways needs further investigation.*

**Key words:** : impacted canines, bracketing, complications

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## INTRODUCTION

Impacted teeth present many problems for the orthodontist.

The second most commonly impacted tooth, after the maxillary third molar, is the maxillary canine [1].

Upper canines can be impacted labially or palatally; palatal impaction of the upper canine exceeds that of labial impaction [2].

Spontaneous eruption of palatally impacted canines without

surgical intervention it is a rare phenomenon [3].

There are various techniques employed to expose impacted canines, from surgical exposure alone allowing spontaneous eruption [4], or surgical exposure and placement of an attachment to facilitate orthodontic traction [5].

Our aim was to compare the complication rate for those types of procedures.

## MATERIAL AND METHOD

The surgical and orthodontic records of 20 palatally impacted maxillary canines were retrospective examined. In ten subjects the ectopic canines were surgically exposed alone (Group 1) and the other ten cases (Group 2) brackets were bonded to facilitate orthodontic traction (Figure 1).

As the cases were consecutively treated the two groups were considered similar for the purposes of this investigation.

The information collected included the treatment mode and complications, including failure of exposure, attachment failure, or failure of eruption.



Fig.1 Clinical aspect of an patient undergoing bracketing  
(Reprinted with permission from Bucur A.: *Compendiu de Chirurgie Oro-Maxilo-Facială*, p. 165. © 2009 by Q Med Publishing, București)

## RESULTS

The mean ages at diagnosis for both groups were considered equivalent. No statistical differences were found between the male and female data.

Complications included failure of exposure, failure of eruption, bond failure and are summarized in Table 1.

The complication rate for the cases which had been bracketed was greater than that for those who were exposed alone.

Six patients (60%) required a second surgical procedure, compared with 3 (30%) of those where simple exposure was used.

Table 1 The complication rate

	Group 1	Group 2
Failure of exposure	2	0
Bond failure	0	2
Failure of eruption	1	4

## DISCUSSION, CONCLUSIONS

This study looked at 10 consecutively treated cases by two different procedures.

The two groups were found to be well matched in terms of age and sex, and were considered equivalent for the purposes of the study, supported the large accepted opinion [6].

Bracketing is a much more technique-sensitive procedure, which is often performed under unfavorable circumstances [7].

The overall complication rate was two times greater in the patients

undergoing bracketing compared with those in whom surgical exposure alone was performed.

Our results sustain a change of the current surgical and orthodontic protocols of the palatally impacted canine [8].

We consider that a prospective study is necessary to assess the efficacy of both methods and to evaluate the long-term evolution of surgical-orthodontic treatment.

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# ROLE OF THE DENTAL HYGENIST IN THE DENTAL PRACTICE

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## ABSTRACT

*Worldwide, prevention gradually starts to gain a primordial role in public health as the task of any medical discipline is to first study the prevention of disease i.e. to ensure a specialized primary prophylaxis.*

*The human body represents an inexhaustible source for medical science and the oral cavity is an “entrance gate”, so we may state that dentistry really holds an important role in the health state of the organism.*

*One of the methods for primary dental prevention is health education. Dental health education is a component of dental medicine linked to the study and implementation of preventive measures of information, training and education of patients and early treatment (at both individual and community level) with the purpose to ensure the integrity of oral-dental structures throughout human life.*

*Scientifically based and rigorously applied preventive dentistry has wide perspectives and an increasing importance in our country as dental caries has become a social disease (very expensive for the society) which justifies the intensive preoccupation to find effective preventive means which are biologically and socially imperative.*

**Key words:** dental hygienist; preventive dentistry; dental caries

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## INTRODUCTION

The role of the dental hygienist, prevention assistant, also becomes an educational one, and in order to be able to create a relation with the patient, the dental practitioner must also have serious knowledge in psychology and pedagogy.

The education given by the prevention assistant must lead to changes in patient behaviour regarding specialized treatment in such a manner to transform the patient into an active

collaborator and “going to the dentist” to cease being associated to pain.

From the moment the patient sits in the dental chair, he or she must be hygienized, educated and psychologically prepared for specialized treatments.

The assistant must always represent a bridge between dentist and patient, she must be determined and open to patients’ problems, always prepared with a warm smile and supportive words.

## DISCUSSION

In Romania, information represents a real problem. In dentistry, communication is very important and with an uninformed patient it becomes increasingly difficult.

Any member of the medical staff has to educate patients, but a wide scale dental health education may only be achieved with external aid: Ministry of Health, Ministry of Education, television, radio, other mass media and companies producing oral hygiene materials.

The initiative must start from the Ministry of Health in collaboration with the Ministry of Education.

The prevention assistant holds an important role in wide scale information of the general public. Outside the dental practice, the prevention assistant contributes to the information and education of the population by giving open lectures in kindergartens, schools, hospitals and other institutions.

Unfortunately, there are insufficient efforts made for implementing dental health education mainly due to lack of resources.

From a dental point of view, health is threatened by 4 types of diseases: dental caries, periodontal disease, dental-maxillary malformations or abnormalities and

cancer. In all these conditions, prevention plays an essential role as prophylaxis (primary prevention) can be effective.

Health education is complex because it must start early in life and must continue constantly with the support of the dental education and profession.

Informative materials should be edited for the entire population in the form of booklets on various themes: dental brushing, risks of excessive sugar consumption, role of fluorides, attending periodic follow-up visits.

There are two more important information means for the population:

- the action of hygiene materials producers
- the use of communication (mass media).

Visual and audio-visual educational materials are the best to fulfil this goal. As such, slides, movies, video tapes must represent the support for transmitting the prevention message together with brochures and illustrated books. Of course, all these materials must be specially designed for children and adults, respectively. This is due not only to the fact that children are different from adults but also to the different way knowledge is acquired: the child will memorize



before understanding while the adult must understand in order to memorize; the child does not have preconceptions or stereotypes while the adult does, based upon previous experience.

There are numerous types of educational materials. The most important are:

- movies;
- video tapes;
- brochures and illustrated books;
- slides.

In principle, any practitioner might prepare a set of slides based upon personal cases to illustrate the consequences of not practicing oral-dental hygiene techniques.

In our country, along with locally edited brochures, several educational books have been elaborated on the topics of teeth and dental care.

There are also self-teaching manuals which can be used by patients to rigorously apply techniques and performing self-control. Of course, such manuals can only be disseminated within human communities where a high degree of civilisation has been reached.

The audio-visual system may be installed in the waiting room, with the

advantage of being able to inform more patients at the same time.

The dental practice is not suitable for slide presentations. The ideal area is the dental prevention room as it is specially designed for this purpose with:

- dental chair for demonstrations, check ups, and individual plaque assessment;
- educational equipment in the field of hygiene and audio-visual system;
- posters or explanatory charts on the walls;
- qualified personnel;

In the same room, the educational brochures and books will be available for the patient.

The efficiency of a dental practice is highly improved by the professionalism and availability of the dental assistant in relation to the patient.

Starting with the tone of the voice during a simple phone call, the warm welcoming smile while receiving patients and concluding with the adequate professional activity, all these indicate the importance of the dental assistant in the dental practice.

## CONCLUSIONS

At present, no collaborative relation can be conceived between assistant and patient without the former possessing solid psychology knowledge. Thus, the assistant has the task of an educator. The education he or she performs must lead to behaviour changes regarding the specialized treatment in such a manner that the patient becomes an active collaborator.

The emotional relationship established between assistant and child (given the fact that our professional activity relies upon prophylactic treatment in children) must develop into a mutual agreement in which the patient feels that success highly depends on him/her. It is crucial that

all treatments in children to be as painless as possible. Prevention of pain may be discussed in pediatric dentistry. This does not mean promising children painless interventions when we ourselves are not convinced. It is far more correct and easy to accept by patients to be told that it will hurt a little.

Several of the tasks of an assistant strictly connected with professional competence will be listed below:

- a) by skilfulness, she or he must achieve a good contact with the patient;
- b) keeping the psychological climate reached during the treatment,

regardless of the degree of patient discomfort;

c) permanent self-control on aggressive trends as well as their expression;

d) capacity for empathy, for understanding the other party's situation which will aid in understanding the patient and will facilitate a good relationship;

e) educational role, by discussing investigation and therapeutic procedures, by explaining the need for certain interventions.

The pleasure to teach others is a real fact. It values the tasks of the

assistant who discovers with great satisfaction the success of motivation. Attached and grateful patients are further reasons for satisfaction. Finally, the feeling of sharing responsibility within the team, providing the dentist with a patient who is suited for dental treatment is a component of the group dynamics which also offers satisfaction.

Oral health promotion must also reach those who did not benefit from oral health education programmes and who do not regularly have access to dental care..

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# OSTEONECROSIS OF THE JAWS IN PATIENTS TREATED WITH BISPHOSPHONATES: AN UPDATE

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## ABSTRACT

*Osteonecrosis of the jaws in patients on long-term bisphosphonate therapy is being reported in the last ten years in the literature with increasing frequency. Management is controversial but there is little evidence basis and the consensus is to be conservative.*

*Our main goal is to review the current literature on BRONJ.*

**Key words:** BRONJ, osteonecrosis, risk factors

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## INTRODUCTION

Bisphosphonate-related osteonecrosis of the jaws (BRONJ) is a severe complication in patients on bisphosphonates treatment for osteoporosis or metastatic malignant disease.

First reports of BRONJ focused on those cases caused by intravenous bisphosphonates used to stabilize bone metastatic malignant disease [1]. Since then, many authors reported osteonecrosis in patients on oral bisphosphonates treatment for osteoporosis and its precursor osteopenia [2].

Osteonecrosis of the jaws in association with bisphosphonates therapy is currently a recognised disease, but the exact pathophysiology of BRONJ remains unclear. Different hypotheses about its pathological mechanism have been offered, such as suppression of bone remodelling or

direct toxicity of bisphosphonates on bone [3].

Currently, the definition and classification of the AAOMS, which was updated in 2009, is widely accepted [4]; exposed bone is the main sign for the clinical confirmation of the specific diagnosis.

It has been shown in the last years that the incidence of BRONJ seems higher in patients with malignant diseases than in patients on oral drugs, but only few studies have investigated a representative number of patients.

Recently, a new bone resorption inhibitors class was introduced in cancer-related skeletal complications: RANKL inhibitor (denosumab, Prolia®). Preliminary studies show that osteonecrosis also occurred in patients receiving denosumab treatment [5].

## RISK FACTORS

Although the aetiological process of BRONJ remains incompletely understood, it seems to be multifactorial. Several risk factors have been established in the literature. Several authors have shown an increase in the incidence of BRONJ in correlation with bisphosphonate type, the duration of treatment or number of doses administered [6]. The role of other drugs used in the treatment of

malignant underlying diseases and glucocorticosteroids as a potential additional risk factors remains unclear.

Dental extractions and implant insertion were clearly shown to increase the risk of BRONJ development. The presence of spontaneous lesions is still questionable [7].

## DIAGNOSIS

Medical history and clinical examination are the most important steps in the decision-making process. The main clinical signs and symptoms

are exposed and necrotic bone with mucosal swelling, abscesses and fistulas (Figure 1).



*Fig.1 Intra-oral image of the affected jaw side revealing ulcerating aspect of the non-healed extraction side*

Bone lesions can be observed especially in the mandible, in the mylohyoid ridge, but quite frequently both mandible and maxilla are involved [1].

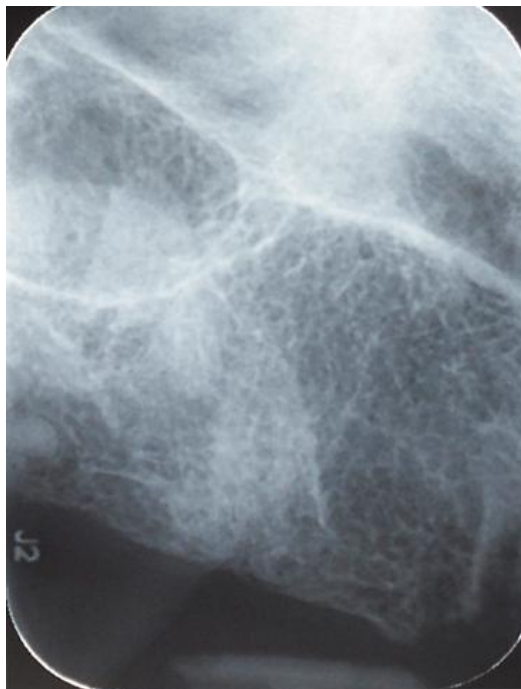
Some authors have suggested the use of carboxy-terminal collagen crosslink (CTX) level for the identification of the affected jawbone. To date, risk prediction by the serum  $\beta$ -CTX level remains debated [8].

Radiography is helpful to assess the bone necrosis, especially in those

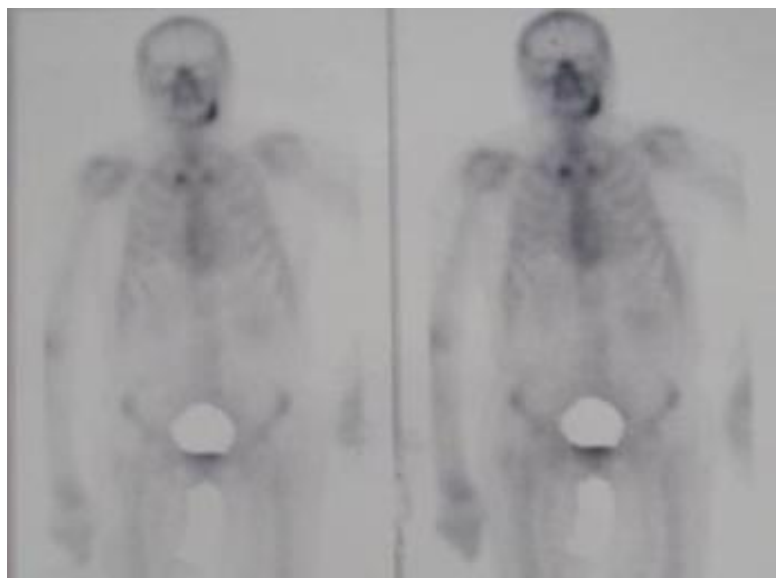
patients with non-exposed bone, showing non-specific findings such as sclerotic changes (Figure 2).

Bone scintigraphy is also an effective tool in early stages [9], though findings are not specific (Figure 3).

Unfortunately, preventive diagnostic imaging is too expensive to use in all patients receiving bisphosphonates and the benefits are questionable.



*Fig.2 Radiography showing sclerotic changes at the alveolar process*



*Fig.3. Scintigraphy showing hotspots in the left mandible*

## TREATMENT

The BRONJ therapy remains an unresolved problem and there are no evidence-based guidelines. Excision of all necrotic and infected bone areas, after 3–6 months of bisphosphonates discontinuation may offer long-term palliation with resolution of acute infection and pain (Figure 4).

Apart from therapeutic measures, preventive dental procedures remain of the utmost importance and have been shown to have positive effect [10]. The laser therapy and hyperbaric oxygen were of no definitive benefit.



*Fig.4. Sequestrectomy after a 6 month drug holiday*

## CONCLUSIONS

After ten years of gathering knowledge in dealing with BRONJ, evidence-based data are still lacking.

The surgical trauma is a recognized predisposing factor to osteonecrosis development. Minimally invasive

surgical treatment appears to be the optimal approach for BRONJ management. There is general agreement on the fact that dental preventive measures in patients being

candidate for or already receiving bisphosphonates treatment are of major importance to reduce the risk of BRONJ development.

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# TREATMENT OF IMPACTED CANINES WITH A COMPLETELY CUSTOMIZED LINGUAL APPLIANCE. A CASE REPORT



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## ABSTRACT

*A completely customized lingual appliance is suited for all kinds of orthodontic therapy including the treatment of impacted teeth. Apart from third molars, the teeth most frequently impacted are the maxillary canines. Often, surgical exposure and orthodontic guidance are required during the treatment process. This article presents a case report of a 15 years old female patient with a impacted canine, treated with a completely customized lingual appliance.*

**Key words:** *Lingual appliance, impacted canine, invisible orthodontic treatment, surgical exposure, torque and angulation control*

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## INTRODUCTION

Among the more frequent tasks in orthodontics is the alignment of displaced or retained teeth. The reasons for the retention of individual teeth can vary greatly. Maxillary canines are often affected. The incidence of retained maxillary canines is 1-2 %. The upper canine is esthetically and functionally very important in human dentition, and it plays a key role in occlusal guidance. There are numerous possible etiological factors for its displacement. For example, the long and complicated eruption path and late

date of eruption are often blamed. The root of the lateral incisor is also thought to play a key role as a "guide rail". Tooth germ displacement, trauma and premature loss of deciduous teeth with mesial migration of premolars with lack of space may come into play. Last but not least, genetic factors have been described. This article presents a case report of a 15 years old female patient with a impacted canine, treated with a completely customized lingual appliance.

## MATERIAL AND METHOD

A 15-year-old female patient with a palatally impacted left maxillary canine tooth presented in our clinic. Moreover, several teeth in the maxilla and mandible showed slight spacing and mild misalignment (Figures 1 to 4). After discussion of the treatment

options with the young patient and her parents, it was decided to use the Incognito™ Appliance System for corrections in the maxilla due to esthetic reasons: the young patient wanted braces that were invisible to others.



Figure 1: The situation prior to orthodontic treatment



Figure 2: The left deciduous maxillary canine is still in place



Figure 3: Mild spacing and misalignment is visible



Figure 4: Occlusal view of the initial situation in the upper arch

In the practice, impressions were taken and sent to Top Service (a special laboratory in Bad Essen / Germany). There, two casts were made. One model was used for a set up. The casts of the initial situation and the set up were scanned with a highly precise 3D device and the customized brackets as well as the individual archwires were designed in a digital procedure. The shape of each bracket was digitally plotted to the lingual surface of the

corresponding tooth to facilitate exact placement in the mouth. For the impacted tooth, a bracket was planned by mirroring of the existing right maxillary canine tooth (Figure 5). Subsequently, the Incognito™ Appliance System was produced and every single part of it – brackets, bracket slots and archwires – underwent different stages of quality control.

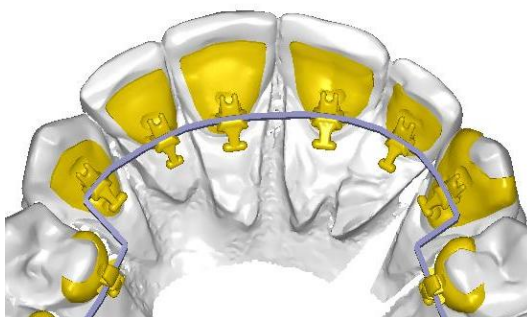


Figure 5: The bracket on the impacted tooth was designed by mirroring of the existing maxillary canine. In this way, the shape of the tooth surface can be predicted.

Afterwards, the system arrived in the practice. The following arch wire sequence was planned: 0.016" NiTi; 0.016 x 0.022" NiTi; 0.016 x 0.022" SS;

0.0175 x 0.0175" TMA. Estimated treatment time was 17 months.

In the first phase of treatment, the brackets were bonded from first molar to first molar in the maxilla and a

0.016" NiTi archwire was inserted. A superelastic push coil was fixed on the brackets of the left lateral incisor and the left first premolar (Figure 6). After a period of approximately four months, the primary canine was extracted. In a

surgical procedure, the impacted tooth was exposed and an eyelet placed on the uncovered surface. The eyelet was attached to the push coil using a power thread in order to extrude the tooth (Figures 7 and 8).



Figure 6: Bonded lingual brackets, archwire and the push coil in place.



Figure 7: Situation after extraction of the deciduous tooth and exposure of the impacted canine. The eyelet is visible on the tooth.



Figure 8: Treatment progress

Ten months after the start of the treatment, the canine tooth was completely erupted and the eyelet was removed. Subsequently, the mirrored bracket, which had been produced at the beginning of the treatment, was bonded on the canine (Figure 9). The treatment continued with a new archwire - 0.016 x 0.022" NiTi - that

was used for derotation, angulation and torque control of the left maxillary canine (Figure 10). The first premolar was excluded from the wire in order to obtain a favorable force. During the following appointment, a powerchain was added (from the right first premolar to the left canine) to start closing spaces (Figure 11).





Figure 9: The mirrored bracket for the left maxillary canine tooth.



Figure 10: Situation after bonding of the bracket on the canine.



Figure 11: Space closure using a powerchain.

<p>14 months after the beginning of the treatment, the last archwire - 0.0175 x 0.0175" TMA - was placed and a</p>	<p>complete powerchain added for space closure, final alignment and finishing in the upper arch (Figure 12).</p>
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Figure 12: Final aligning of the upper arch.

## RESULTS

After debonding of the appliance system, it became clear that a remarkable improvement had been achieved. The planned treatment result

– recorded in the set up – was obtained and the patient and her parents were highly satisfied with the esthetic appearance (Figures 13 to 16).



*Figure 13: The final result*



*Figure 14: The previously impacted canine in its ideal position to allow for anterior guidance*



*Figure 15: Spacing and misalignment were eliminated*



*Figure 16: A satisfactory result was obtained*

## DISCUSSION

This case report illustrates the treatment of a displaced upper canine with a completely customized lingual appliance. Due to great importance of the canine as regards dental esthetics

and functional occlusion, any decision to extract should be carefully weighted. Reliable and predictable treatment outcomes could be achieved using a customized lingual appliance.

## CONCLUSIONS

Alignment of impacted canines with lingual orthodontics has many

advantages for the patient and orthodontist.

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# ANALYSIS OF HEMOLYTIC BACTERIAL AEROSOL CONTAMINATION IN DENTAL PRACTICE



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## ABSTRACT

*High speed instruments are aerosolizing from patient's mouth oral fluids, blood and other secretions and calculus and are exposing medical personnel from dental office to potential infectious diseases. METHOD 720 air samples in 80 working days of 4 dental offices were collected prior patients arrival and after 4 hours of regular dentistry interventions and treatments. RESULTS Significant increases in final TNG with hemolysis were found in dental offices treating more than 5 patients in the 4 hours time interval, when accounting initial TNG with hemolysis. CONCLUSIONS The exposure to hemolytic germs of medical personnel from dental offices is higher when more patients per time interval are treated, increasing the risk of infection.*

**Key words:** hemolytic microbial aerosols, dentist, risk of infection

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## INTRODUCTION

Despite recent advances in dentistry, medical personnel working in dental offices are still exposed to infectious diseases caused by bacteria, viruses, fungi and prions aerosolized by dental procedures, brought inside by patients and staff portage, and due to environment and air-conditioning systems at higher levels than years ago. This is mostly caused by usage of higher speed instruments. Instruments such as turbines, micro-motors, air-water syringes and ultrasound scalers are producing aerosols and spatter from oral fluids, blood and other secretions and calculus [1-3].

Depending on their size, aerosolized particles can remain suspended in the air for long periods of time, while they can be inhaled by

medical personnel. They tend to settle in time and can contaminate surfaces, floors and instruments left uncovered, and then can be lifted again in the air due to air turbulences. Most of pathogens have aerodynamic diameters of 2-10  $\mu\text{m}$  and settle quickly on surfaces due to gravitational forces. For example, a 10  $\mu\text{m}$  diameter particle with a density of a unit will fall 1 m in 5.5 minutes in an undisturbed environment, and a particle with 5  $\mu\text{m}$  diameter will fall 1 m in 21 minutes, in the same environment [4].

The aim of this study is to analyze alterations in the total number of hemolytic germs in 4 dental practices accounting initial values and the number of patients treated in the meantime.

## MATERIAL AND METHOD

The study took place in 4 dental practices and a total of 80 days with activity were included in the analysis. Air samples were taken into 2 distinct moments of the day: before the patient arrived and after 4 hours of activity. Sampling on each occasion was performed on 3 different Petri plates that contained 3 different culture medium: agar, blood agar 5% and Sabouraud, resulting a collection of 720 air samples.

For air sampling we used M.A.Q.S (Microbiological air quality sampler - Oxoid). The air is sucked by the turbine through a perforated filter. Air flow is directed to the Petri plate, situated under the grill. The air volume is 100 l/minute and for each sample is recommended the sampling of maximum 1.000 liters of air. Exciding

this quantity will dehydrate the surface of Petri plate.

All plates were labeled and transported to the Microbiology laboratory. All plates were incubated 24 hours at 37°C. We used the following bacteriological indicators: the total number of bacteria (CFU/m<sup>3</sup>), and the total number of hemolytic bacteria (CFU/m<sup>3</sup>) and the total number of fungi (CFU/m<sup>3</sup>).

For this article we used only data concerning hemolytic bacteria.

Data were processed using IMB SPSS version 18 (2010). For the initial comparisons between dental offices of TNG with hemolysis we used ANOVA with Turkey post-hoc analysis and the analysis of covariance for the determination of the alterations in final TNG with hemolysis when accounting the initial TNG with hemolysis.

## RESULTS

Initial total number of hemolytic germs (TNG) is ranging between 2 and

22 CFU/m<sup>3</sup> with a mean of 10.68 CFU/m<sup>3</sup> and a standard deviation of



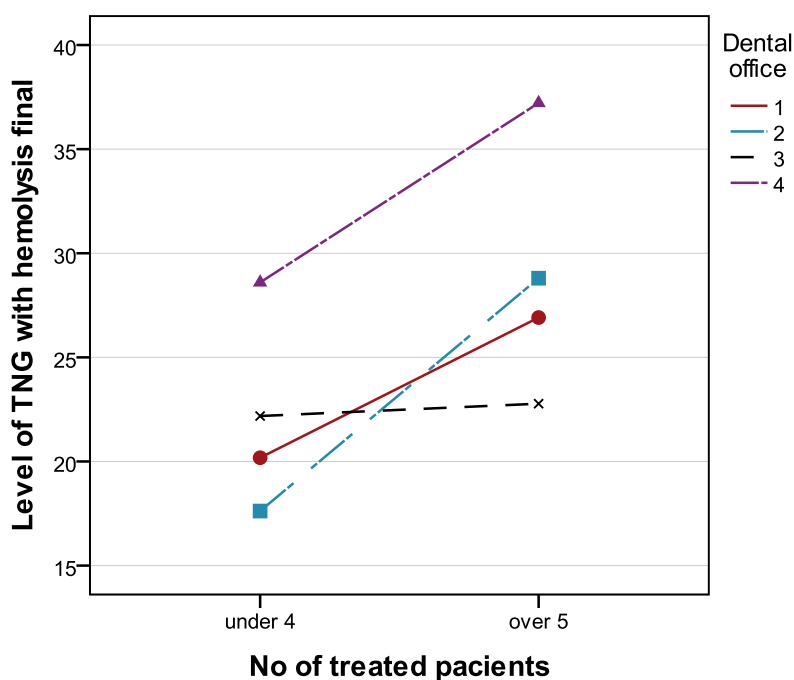
4.75. Initial values of TNG with hemolysis is not significantly different between dental practices,  $p>0.05$ .

Mean final values, after 4 hours of regular dental activity were  $25.5 \pm 11.43$  CFU/m<sup>3</sup>. A 2 by 2 between-groups analysis of covariance was conducted to assess the influence of dental office and the number of patients treated during the 4 hours of activity on the level of final TNG with hemolysis. Initial TNG with hemolysis were introduced in the model as covariates, to control for initial difference between practices.

After adjusting for initial values, significant differences of TNG with hemolysis were observed among dental practices  $F(3.79)=4.32$ ,  $p<0.01$ ,  $\eta^2=0.15$ . Dental practice no 4 has the

mean value of TNG with hemolysis significantly higher than those of dental practice no 1 (mean difference=9.36 CFU/m<sup>3</sup>), no 2 (mean difference=9.69 CFU/m<sup>3</sup>), respective no 3 (mean difference =10.42 CFU/m<sup>3</sup>). Differences between other practices were not statistically significant,  $p>0.05$ .

After adjusting for initial values, significant differences of TNG with hemolysis were observed when more than 5 patients were treated in the 4 hours time interval  $F(1.79)=7.46$ ,  $p<0.001$ . Mean difference between the group with more than 5 patients when compared to the group with less than 4 patients was 6.78 CFU/m<sup>3</sup>. Size effect  $\epsilon=0.09$ , is small, according to Cohen (Figure 1).



Covariates are evaluated at the following values: NTG with hemolysis initial = 10,68

Figure 1. Distribution of final TNG with hemolysis in relation to the number of treated patients when accounting to initial TNG with hemolysis

## DISCUSSIONS AND CONCLUSION

Mean initial values of TNG with hemolysis were  $10.68$  CFU/m<sup>3</sup>  $\pm 4.75$ CFU/m<sup>3</sup>. Mean final values, after 4 hours of regular dental activity were  $25.5 \pm 11.43$  CFU/m<sup>3</sup>. The difference between initial and final values is

caused by portage caused by medical personnel and patients, and due to aerosolization of bacteria from patients' saliva, blood and calculus during dental procedures.

Other researchers found significant increases of mean number of mezophilic germs after dental treatments in trial performed in Iași, Romania [5]. Similar results were published by Azari and colleagues [6], that the total bacterial counts in the air of dental surgery rooms and in non-surgery rooms without direct involvements with dental operations were in the range of 120-280 CFU/m<sup>3</sup> and 49-128 CFU/m<sup>3</sup> respectively.

We have observed significant increases in NTG with hemolysis in practices with more than 5 patients treated during the 4 hours interval. Most incriminated bacteria in producing hemolysis are Staphylococci, Streptococci and *P. aeruginosa*.

*Staphylococcus aureus* is an opportunistic bacterial pathogen associated in healthy individuals with asymptomatic colonization of the skin and mucosal surfaces. Depending on host susceptibility and the aggressiveness of the strains, it also can be the cause of wound infections and has the potential to induce osteomyelitis, endocarditis and bacteremia, leading to infections in any of the major organs of the body. It also is responsible for many serious community- and nosocomially-acquired infections, being the most frequently isolated bacterial pathogen from patients with hospital-acquired infections, especially patients with implants or prosthetic devices [7-9]

*Streptococcus pyogenes* (group A streptococcus, GAS) is an important species of Gram-positive extracellular bacterial pathogen which colonizes the throat or skin and is responsible for a broad spectrum of diseases that range from simple and uncomplicated pharyngitis and skin infections

(impetigo, erysipelas, and cellulitis) to scarlet fever and life-threatening invasive illnesses including pneumonia, bacteremia, necrotizing fasciitis, streptococcal toxic shock syndrome (TSS), and nonsuppurative sequelae such as acute rheumatic fever, reactive arthritis and glomerulonephritis[10,11].

*Pseudomonas aeruginosa* is ubiquitous in water, vegetation and soil. *Pseudomonas aeruginosa* is primarily a nosocomial pathogen. According to the CDC, the overall incidence of *P. aeruginosa* infections in U.S. hospitals averages about 0.4 percent (4 per 1000 discharges), and the bacterium is the fourth most commonly-isolated nosocomial pathogen accounting for 10.1 percent of all hospital-acquired infections. *Pseudomonas aeruginosa* is incriminated in the infectious pathology of many systems of the body, including skin, ears, eyes, wounds, bones and joints, the lungs, heart, central nervous system and the urinary tract. Most exposed to opportunistic infection with *P. aeruginosa* are certain vulnerable populations, such as those patients who are severely immune-suppressed, those with indwelling urinary, intravenous and other catheters, those with open wounds or pressure sores, those with severe burns and those with cystic fibrosis [12].

The risk of infections is increased in the presence of aerosolized hemolytic germs. The aerosols can be inhaled and can produce local, into respiratory tract and general spread of bacteria. Hemolytic bacteria can also infect open wounds present on unprotected and uncovered skin [1-3].

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# ORAL ENVIRONMENT IN STRESSFUL CONDITIONS



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## ABSTRACT

Dental decay is a bacterial infectious disease, which results into irreversible localized destruction of dental structures. The aim was to investigate some salivary parameters involved in tooth caries.

**Material and method.** There were investigated some salivary factors involved in tooth decay in a group of students aged 20-23 years (35 cases). The subjects were clinically investigated and was noted DMF index (D- decayed, M- missing, F- filled). The students provided stimulated saliva samples before and immediately (5 minutes) after a stressful condition represented by a difficult exam. There were noted salivary volume and salivary flow/minute. The buffer capacity was determined with Dentobuff® Strip kit from VIVACARE.

From salivary sediment were determined the number of leukocytes, epithelial cells and cell viability with tripan blue dye (under microscope the cells which exclude the dye are viable) expressed as percent. To compare the results t Student test was performed. Were compared the mean values of investigated parameters before and after the exam.

**Results.** The salivary volume ( $4.1 \pm 1.02$  ml), salivary flow ( $0.82 \pm 0.2$  ml/min) and pH ( $7.1 \pm 0.54$ ) were decreased before the exam, probable due to sympathetic stimulation associated with the increase of salivary mucus. The increased salivary flow ( $1 \pm 0.49$  ml/min) after the exam was correlated with increased pH ( $7.6 \pm 0.54$ ). The leukocytes number slightly decreased after the exam. The increased number of epithelial cells after the exam (from  $128 \pm 61.4/\text{mm}^3$  to  $142 \pm 14.6/\text{mm}^3$ ) was correlated with the decrease of cellular viability (from  $86 \pm 10.83\%$  to  $81.6 \pm 10.96\%$ ). This can induce a decrease in the function of protective barrier represented by oral epithelium.

**Conclusions.** The increase of salivary flow, pH and cellular viability is a sign that the body responds with a defense reaction to stress. But prolonged stress can produce a decrease of body defense which can exacerbate cariogenic bacterial virulence in oral cavity. **Key words:** stress, salivary cells, microorganisms, caries

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## INTRODUCTION

Dental caries is a most common reality in dental practice, found in patients of all ages and social environments. Dental caries is an infectious disease, which results in localized dissolution and irreversible destruction of dental tissues [1]. The etiological agent for decay is colonized dental plaque, which is a soft layer, strongly adhered to teeth surfaces. The plaque is colonized with Gram positive bacilli, Gram negative bacilli, fusobacterias, filamental bacterias and spirochets [2].

The saliva has a strong influence on dental cavity pathogeny through it's characteristics:

- Mechanical cleaning, an important but insufficient mechanism for removal of plaque [3],

- Reduce the solubility of the enamel by a continuous ion exchange [4],

- Local neutralizing effect through salivary buffer systems,

- Low antibacterian activity, assured by the presence of lysosime, lactoperoxidasis, and immune system (IgA antibody) [5],

- Salivary pH: the increase of salivary acidity acts on tooth favorises enamel demineralization [6],

- Quantity: in salivary glands aplasia, or in xerostomia results a type of cavity with rapid evolution. A large volume of saliva favorises mechanical cleaning and the action of buffer systems.

The aim of this study was to investigate the effect of stressful condition on oral environment.

## MATERIAL AND METHOD

In this study were investigated the main salivary factors involved in cavities in: a group of students aged 20-21 years (17 cases -groupe 1); a group of students aged 22-23 years (18 cases - groupe 2). All students were examined and DMF index (D- decayed, M-missing, F- filled) was determined.

Saliva is a clinically biological fluid that is useful for novel approaches into prognosis, diagnosis, monitoring and management of patients with both oral and systemic diseases. It is easily collected and stored and ideal for early detection of disease as it contains specific soluble biological markers (biomarkers). Saliva contains multiple biomarkers which make it useful for multiplexed assays that are being developed as rapid tests, or in more standardized formats for centralized clinical laboratory operations [4]. Salivary diagnostics is a dynamic field that is being incorporated as part of disease diagnosis, clinical monitoring and for

making important clinical decisions for patient care [7]. Whole saliva can be easily collected with stimulating agents (using paraffin for mastication, using citric acid or sour candy drops on the tongue) or without stimulation.

Stimulated saliva samples were obtained by chewing a paraffin tablet before and immediately after an important exam (in the first 5 minutes after the exam).

Salivary volume and flow

The salivary volume and flow obtained after mastication was measured and salivary flow was calculated:  $\text{salivary flow ml/min} = \frac{\text{salivary volume (ml)}}{5\text{minutes}}$ .

Buffer capacity and salivary pH

Salivary buffer capacity was determined with Dentobuff® Strip kit from VIVACARE.

Principle: The strip test contains an acid and a pH indicator. The saliva dissolves the acid and the initial pH will be low. If the saliva can buffer the acid the pH will rise. The indicator reflects

the final pH on the strip. The control is a drop of water which will color the strip in yellow, because water has no buffer capacity. This test allows differentiating the buffer capacity into low, medium, and high.

The microbiological study of saliva

Streptococcus Mutans in saliva. From the samples was determined the quantity of Streptococcus Mutans using DENTOCULT SM kit, with the technique provided by producer. The test measures the quantity of Streptococcus Mutans in saliva (which shows the number of colonized tooth surfaces) based on two properties: the streptococcus mutans, unlike other bacteria, can develop in environments with high concentrations of sucrose and bacitracin; can adhere on rough surfaces as the test strip.

Lactobacillus Acidophilus in saliva. From the samples was determined the quantity of

Lactobacillus Acidophilus using DENTOCULT LB kit provided by VIVACARE.

The study of salivary cells

Salivary samples were centrifugated for 5 minutes at 2500 rotations/min. From the salivary sediment was determined the following parameters:

- The number of leukocytes on Burker test plate, using the same principle as for blood leukocytes. The result was expressed in No/mm<sup>3</sup>, [8];

- The number of epithelial cells. The result was expressed in No/mm<sup>3</sup>;

- Cellular viability - with tripan blue dye was determined, on microscope, the ratio of cells which exclude the dye (alive, uncolored cells). The ratio of live cells was expressed as percentage (%).

Statistical analysis. The results were analysed and was calculated the mean value (M), standard deviation (SD) and standard error (SE). The values were compared using a t Student's test for paired data, and values of  $p < 0.05$  were considered statistically significant. Were compared the mean values of the students' groups before and after the exam. The statistical correlation was performed by Pearson test.

## RESULTS

From the first group of students was selected 5 students and the following parameters were determined: stimulated salivary volume, flow, salivary pH before and

after having the exam. The results are shown in table 1.

Salivary cells expressed in number of cells /mm<sup>3</sup> and cellular viability, correlated with the exam are showed in table 2.

Table 1. Salivary volume, flow, pH before and after the exam (5 cases)

Case	Salivary volume		Salivary flow		pH	
	Before	After	Before	After	Before	After
1.	5	3,7	1	0.7	7.5	8
2.	2.5	2.5	0.5	0.5	6.5	7
3.	5	9	1	1.8	6.5	7
4.	4	5	0.8	1	7.5	8
5.	4	5	0.8	1	7.5	8
M	4.1	5.04	0.82	1	7.1	7.6
SD	1.024	2.44	0.20	0.49	0.54	0.54
SE	0.458	1.09	0.091	0.22	0.24	0.24

Legend: M= mean, SD= standard deviation, SE= standard error.

Table 2. The salivary cells in students group before and after the exam (5 cases)

Case	Leukocytes		Epithelial cells		Viability	
	Before	After	Before	After	Before	After
1.	220	150	110	50	95	90
2.	150	70	200	100	80	70
3.	30	20	50	40	70	70
4.	120	80	180	120	95	93
5.	80	200	100	400	90	85
M	120	104	128	142	86	81,6
SD	71.76	70.92	61.40	148	10.83	10.96
SE	32.09	31.71	27.45	66.211	4.87	4.9

Legend: M= mean, SD= standard deviation, SE= standard error.

In order to analyse the results on studied groups, statistical comparisons were performed on all determined parameters (table 3).

There were found positive correlation between variations of salivary leukocytes' number, epithelial cells, and cells' viability. The correlation between viability and pH was very strong, both pre ( $r = 0.926$ ) and post exam ( $r = 0.964$ ). No significant correlation between salivary

volume and pH ( $r = -0.161$ ) after the exam. The correlation of pH after the exam was very strong ( $r = 1$ ) compared with before the exam values.

To both students groups (20-21 and 22-23 yers) was performed a screening test using the VIVACARE kits. Was determined the quantity of Streptococcus Mutans, Lactobacillus Acidophilus, and salivary buffer capacity. The results are presented in table 4.

Table 3. The comparison of salivary parameters before an after the exam

Before exam	Salivary volume	Salivary flow	pH	Leukocytes	Epithelial cells	Viability
M± SD	4.1± 1.024	0.82± 0.20	7.1±0 .54	120±71.76	128±61.40	86±10.83

After exam	Salivary volume	Salivary flow	pH	Leukocytes	Epithelial cells	Viability
M± SD	5.04± 2.44	1±0.49	7.6±0 .54	104±70.92	142±148	81.6± 10.96
t calculated	0.8	0.76	1.46	0.36	0.20	0.64
p significance	0.44 NS	0.46 NS	0.18 NS	0.732 NS	0.85 NS	0.54 NS

Legend: NS- not significant

Table 4. Screening microbiological test

No. cases	Age	Salivary flow	Streptococcus Mutans			DMF	
			I	II	III		
18	20-21	1.2-1.6 ml	8	4	6	1.56	
			44.45%	22.22%	33.33%		
17	22-23	1.4-1.8 ml	15	2	-	1.93	
			88.24%	11.76%	-		
No. cases	Age	Salivary flow	Lactobacillus Acidophilus			Vivacult	DMF
			I	II	III		
18	20-21	1.2-1.6 ml	14	4	-	1+	1.56
			77.78%	22.22%	-	5.55%	
17	22-23	1.4-1.8 ml	16	1		-	1.93

			94.11%	5.89%		-	
No. cases	Age	Salivary flow	Dentobuff			DMF	
			Medium capacity	Low capacity	High capacity		
18	20-21	1.2-1.6 ml	12	4	2	1.56	
			66.66%	22.23%	11.11%		
17	22-23	1.4-1.8 ml	15	1	1	1.93	
			88.24%	5.88%	5.88%		

## DISCUSSIONS

Low salivary cells viability shows a long remaining of cells in oral medium, in which time they die and are disintegrated [9]. From the disintegration of the cells enzymes are released in oral environment enzymes [10], which can initiate and maintain gingival inflammation, at the investigated groups. Gingival inflammation can be favored by hormonal changes specifically in pubertal period [11]. Salivary leukocytes can destroy periodontal bacteria [12].

Saliva normally has a pH of 6.3, but could be modified by the oral health [13]. If salivary pH is diminished the enamel demineralization can increase [14]. There is no exact pH value at which demineralization begins, it may vary between 5.5 - 5.0 (critical pH). This is a very large range because the demineralization is stimulated according to local pH and duration of

exposure to the acid environment [15], [16]. The concept of critical pH is applicable only to solutions that are in direct contact with the enamel. The enamel continuously mineralizes and demineralises according to local pH and local concentration of  $\text{Ca}^{2+}$  6.

Stimulated salivary volume, flow and pH in students group were lower before compared with after the exam (fig. 1). This fact can be explained through the activation of the sympathetic nervous system before the exam. The increase of salivary flow after the exam was correlated with the increase of the salivary pH.

The increase in salivary flow, pH and the decrease in cellular viability are the signs that the organism responds with a defence reaction at all levels in stressful conditions. However, prolonged stress produces a decrease in defence capacity which can exacerbate bacterial virulence in oral cavity [17].

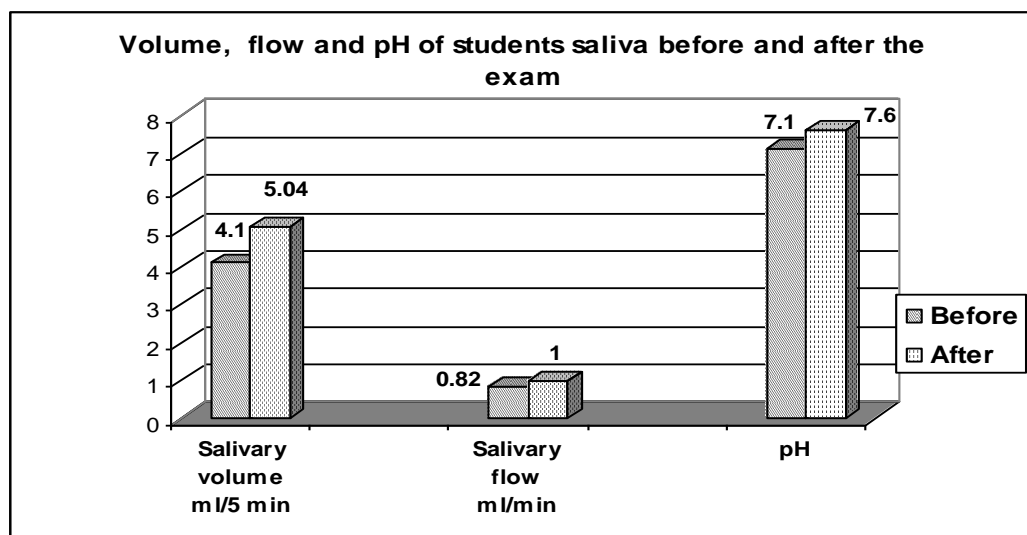


Fig.1. Stimulated salivary parameters in students before and after the exam



The periods with intense sympathetic solicitation through the decrease of salivary flow and pH can have a negative effect on oral immune environment and can favorise the cariogenic activity [18].

Although the number of salivary leukocytes decreased in students after the exam (fig. 2), the increase of epithelial cells after the exam may show an elevated desquamation rate of the oral epithelium as a result of an increased salivary viscosity. The activation of the sympathetic nervous system, in the periods with increased mental activity determines a secretion of saliva with increased mucus.

Increased rate of oral epithelium desquamation was associated with a decrease of cellular viability ( $r = 0.379$ ). This can induce a decrease in barrier function of oral epithelium. The increase of salivary cells was associated with the decrease of cellular viability in

students after the exam. Epithelial cells from the lining of the oral cavity can be found in saliva, but the quantity of epithelial cells from crevicular fluid or pocket is not known [19].

After the exam salivary leukocytes were decreased in our experiment.

The number of leukocytes in saliva varies from person to person, and cell counts vary for an individual during the course of the day, correlated with the timetable. The majority of salivary leukocytes enter the oral cavity via the gingival crevice, through diapedesis. During the initiation of an inflammatory response in the periodontal connective tissue, numerous cytokines, such as prostaglandins, interleukins and tumour necrosis factor-alpha are released from cells from connective tissue fibroblasts, macrophages and polymorphonuclear leukocytes [19].

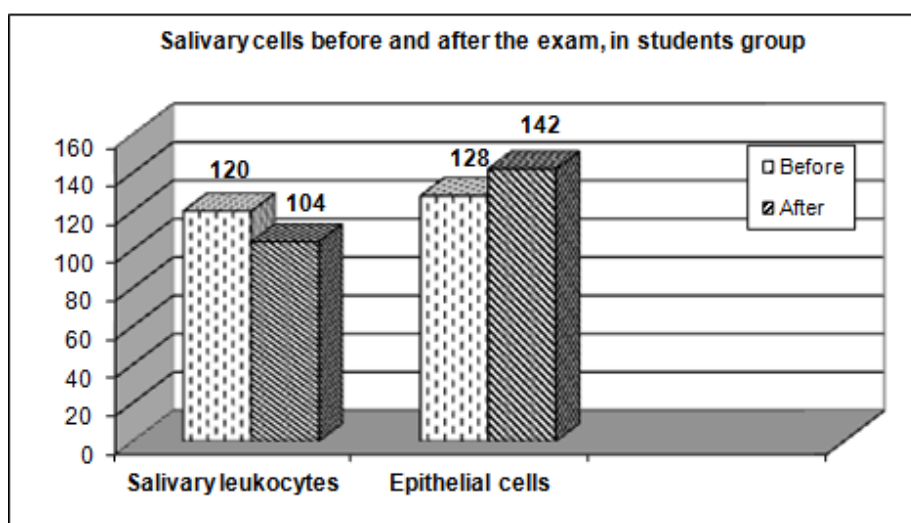


Fig. 2. Salivary cells in students, before and after the exam

The DMF index was correlated with salivary parameters. The high DMF index was associated with low buffer capacity, low salivary flow and low pH. All these showed an increased susceptibility for dental caries.

Were observed a decrease in caries number in students aged 23-24 years compared with students aged 21-22 years probably because an increased interest for oral health. Increased salivary cells in students can be

produced by a poor oral hygiene, which can be a risk factor for caries. Therefore, the students were advised for better hygiene in stressful conditions and supplementary means of oral hygiene.

The kits for Streptococcus Mutans and Lactobacillus Acidophilus are usable in every day dental practice and are useful to determine the risk for cavity and the efficiency of prophylactic treatment.

## CONCLUSIONS

Based on the results were formulated the following conclusions:

- The saliva sample can be used as a prognostic test for dental caries susceptibility.
- In both groups was noted an increase of salivary parameters after the exam, which demonstrate that the stress induced by the exam has an influence on oral environment.
- The increase in salivary flow, pH and the decrease in cellular viability is a sign that the organism responds with a defence reaction at all levels in stressful conditions.

However, prolonged stress produces a decrease in defence capacity which can exacerbate bacterial virulence in oral cavity.

- Is indicated a better hygiene in stress conditions and supplementary means of oral hygiene.
- The kits for *Streptococcus Mutans* and *Lactobacillus Acidophilus* are usable in dental practice and are useful to determine the risk for cavity and the efficiency of prophylactic treatment

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# ASSESSMENT OF CHILDREN AND ADOLESCENTS' INTEREST IN PERSONAL APPEARANCE AND KNOWLEDGE ON ORTHODONTIC TREATMENT



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## ABSTRACT

*The objective of this research was to develop and to apply a questionnaire to assess the level of knowledge of children and adolescents on orthodontics in terms of separate entity within dentistry and their concerns about personal appearance with reference to the aspect of their teeth. The pilot study included 951 children and adolescents from 10 different schools in Oradea, aged 7-18 years, mean age 12.65, standard deviation 3.94 and the gender distribution: 485 boys (50.9% ) and 466 girls (49.1%). We divided this sample into three groups. We analyzed each of the three groups in terms of the importance each student shows for the investigated body characteristics. The physical feature on top of their preferences was scored with 1 in the questionnaire. Thus, in the age group 7-10 years, 220 children considered eye colour as the most important (scored with 1 in the questionnaire), 120 children marked with 1 hair appearance and height etc. There were frequent situations when students marked with the same importance two or more physical features (scored with 1 simultaneously). There are several shortcomings and deficiencies of the educational system regarding the importance of the orthodontic treatment. Thus, over 80% of the primary school children that I questioned did not make the difference between a dentist and an orthodontist. Almost 50% of the secondary and high school students did not make this difference.*

**Key words:** orthodontics, knowledge level, personal appearance

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## INTRODUCTION

In childhood, behaviour has certain fundamental characteristics that distinguish it from the behaviour encountered in higher ages, so it requires specific psychodiagnostic tools. The development and application of questionnaires to this age group should take into account that a child has limited possibilities of focusing his attention, so the act of measurement shall not rely on too many items. [1]

Although each child has individual physical characteristics, there are some basic aspects that are generally valid. Based on this premise, we conducted at a first stage of the research a pilot study where we included a questionnaire that is part of the screening measurement instruments/ categoria instrumentelor de măsurare de tip screening. We

performed this pilot study following the observations made on parents with children who requested orthodontic service, being sent by doctors of general dentistry, and who reported that they were not aware of the existence of orthodontists specialist.

### Objective

The objective of this research was to develop and to apply a questionnaire to assess the level of knowledge of children and adolescents on orthodontics in terms of separate entity within dentistry and their concerns about personal appearance with reference to the aspect of their teeth.

This investigation is meant to create special programmes for educational and therapeutic intervention.

## MATERIAL AND METHOD

The pilot study included 951 children and adolescents from 10 different schools in Oradea, aged 7-18 years, mean age 12.65, standard deviation 3.94 and the gender distribution: 485 boys (50.9% ) and 466 girls (49.1%). We divided this sample into three groups:

- group 1 - 280 pupils aged 7-10 years (primary school), gender distribution: 144 boys (51.42%) and 136 girls (48.57%)

- group 2 - 332 pupils aged 11-14 years (secondary school), gender distribution: 164 boys (49.39%) and 168 girls (50.61%)

- group 3 - 339 pupils aged 15-18 years (high school), gender distribution: 177 boys (52.21%) and 162 girls (47.79%).

Within this research we have conceived the following questionnaire for children and adolescents:

1. For me the following aspects of my appearance are more important (please give marks from 1 to 5 in order of

importance, 1 being number 1 in your preferences):

- A. height
- B. weight
- C. tooth aspect
- D. hair aspect
- E. eye colour

2. The doctor who treats your teeth is also the doctors who aligns them:

- A. yes
- B. no

3. The doctor who aligns your teeth is:

- A. the dentist
- B. the orthodontist
- C. the paediatrician
- D. the family doctor

4. Were you aware of the existence of different appliances to align teeth?

- A. yes
- B. no

5. Would you wear an orthodontic appliance (to align your teeth)?

- A. yes
- B. no

- C. *do not know*
6. *Would an orthodontic appliance cause you any inconvenience?*
- A. *while eating*
- B. *while speaking*
- C. *while smiling*
7. *Have you been told by parents or friends that your teeth are not aligned?*
- A. *yes*
- B. *no*
- The evaluation items included in this questionnaire were adapted to the

particularities of the vocabulary that is specific to childhood correlated with specific problems encountered in the orthodontic practice.

The questionnaire was applied in educational establishments: 15 classes of 2<sup>nd</sup> - 4<sup>th</sup> grade (primary school), 15 classes of 5<sup>th</sup> - 8<sup>th</sup> grade (secondary school) and 15 classes of 9<sup>th</sup> - 12<sup>th</sup> grade (high school).

## RESULTS

The values reflecting average age, standard deviation and gender distribution for the 3 groups of the sample of children and adolescents are presented in table 1.

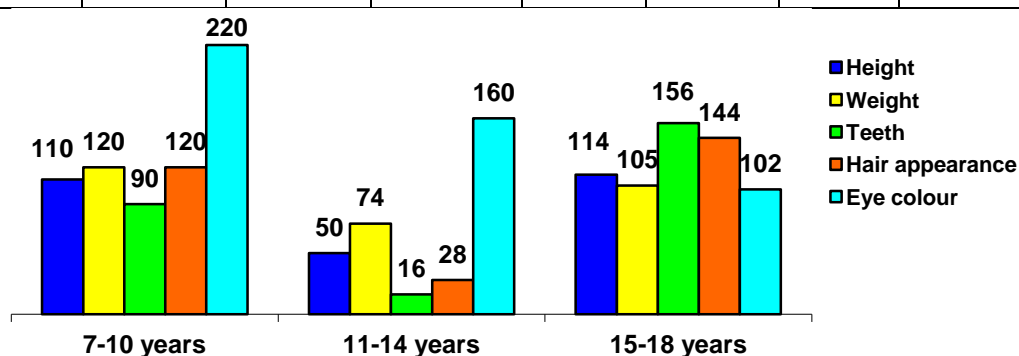
We analyzed each of the three groups in terms of the importance each student shows for the investigated body characteristics. The physical feature on top of their preferences was scored with 1 in the questionnaire. Figure 1 presents a graphical representation of the features of personal appearance rated as most important. Thus, in the age group 7-10 years, 220 children considered eye colour as the most important (scored

with 1 in the questionnaire), 120 children marked with 1 hair appearance and height etc. There were frequent situations when students marked with the same importance two or more physical features (scored with 1 simultaneously). Figures 2 and 3 present the same graphical representation by gender.

Due to the specific of our research, we continued with the analysis of the importance that the preference for the dental aspect holds among the children and adolescents of the 3 age groups. Results are shown in fig.4.

**Table 1.** Structure of the 3 groups according to age and gender

Type of group	No. of subjects	Average age	Standard deviation	Gender			
				Male	Female	Male %	Female %
Group 1	280	8.71	1.11	144	136	51.42%	48.57%
Group 2	332	12.67	1.17	164	168	49.39%	50.61%
Group 3	339	16.59	1.14	177	162	52.21%	47.79%



**Fig 1.** Repartition of subjects according to age groups and to the physical feature appreciated as the most important

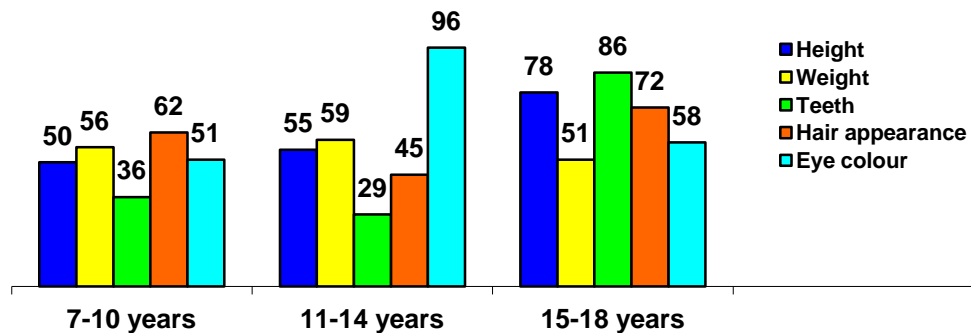


Fig 2. Repartition of the male subjects from the 3 groups according to the physical feature appreciated as the most important

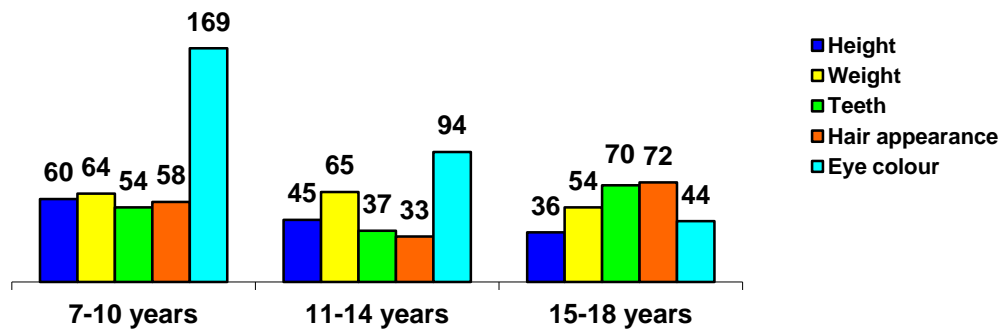


Fig 3. Repartition of the female subjects from the 3 groups according to the physical feature appreciated as the most important

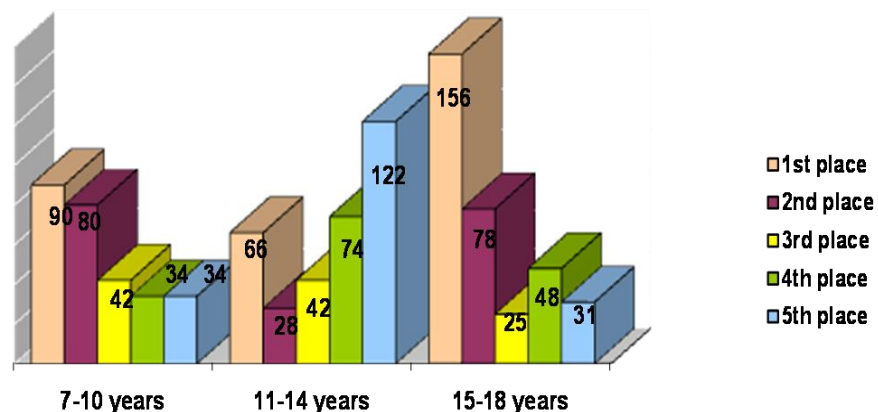


Fig 4. Repartition of the subjects of the 3 groups according to their dental appearances

Then we analyzed the answers given by the students for each item separately, according to age and

gender groups. Results are shown in figures 5, 6, 7, 8, 9, 10.

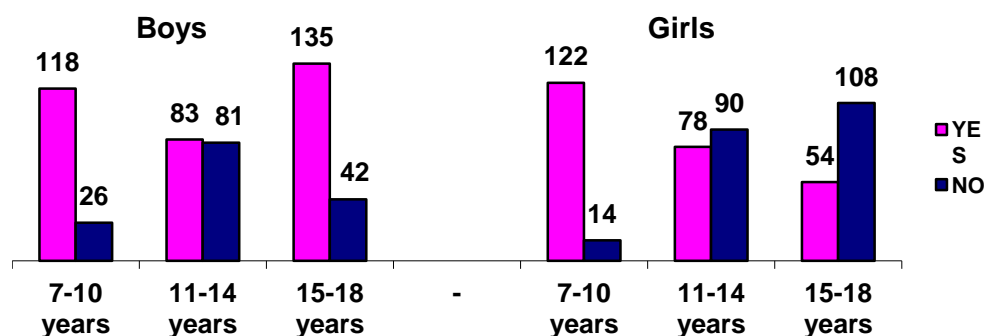


Fig 5. Repartition of subjects, on age and gender groups, according to the answer to the question: "The doctor who treats your teeth is also the doctors who align them"



Fig 6. Repartition of subjects, on age and gender groups, according to the answer to the question: "The doctor who aligns your teeth is"

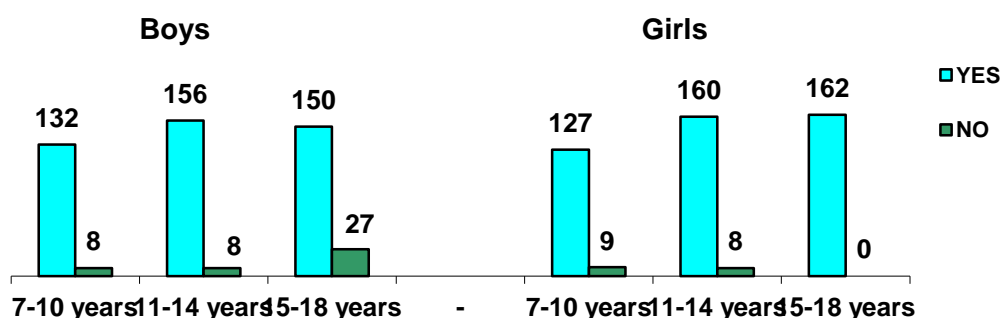


Fig 7. Repartition of subjects, on age and gender groups, according to the answer to the question: "Were you aware of the existence of different appliances to align teeth?"

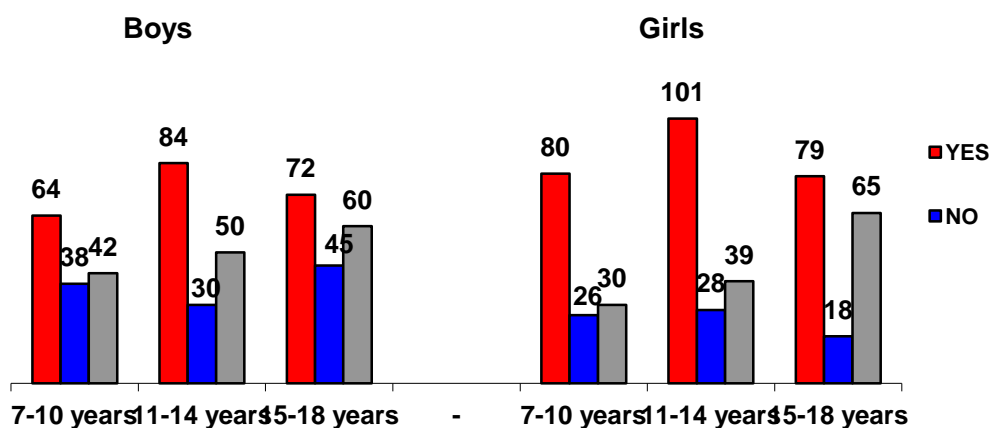


Fig 8. Repartition of subjects, on age and gender groups, according to the answer to the question: "Would you wear an orthodontic appliance?"

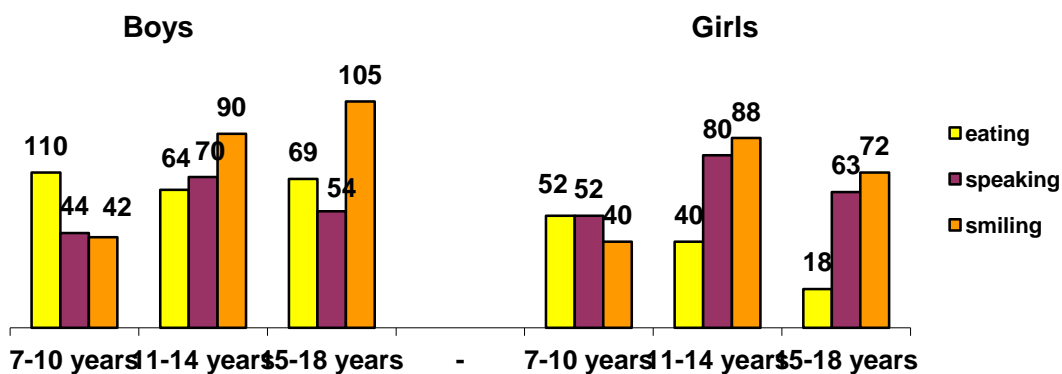


Fig 9. Repartition of subjects, on age and gender groups, according to the answer to the question: "Would an orthodontic appliance cause you any inconvenience?"



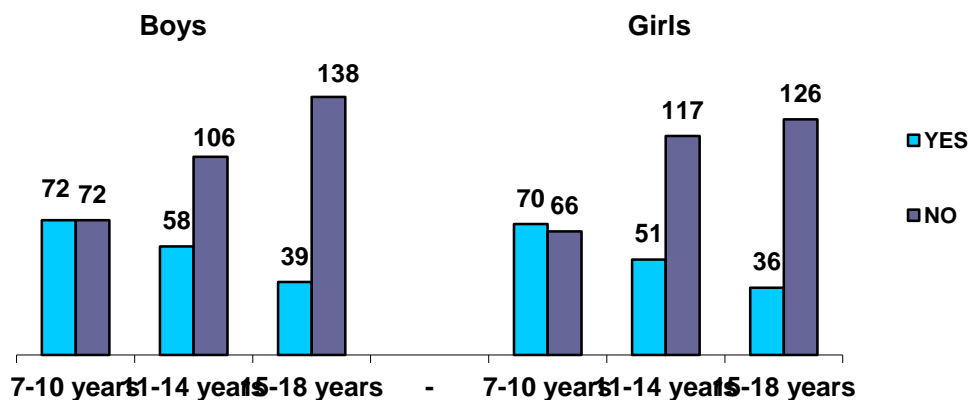


Fig 10. Repartition of subjects, on age and gender groups, according to the answer to the question: "Have you been told by parents or friends that your teeth are not aligned?"

## DISCUSSIONS

This screening type study allowed us to make some considerations on children and adolescents' general and specific - orthodontics - knowledge.

In an overall analysis of the graphic in figure 1 it appears that all students in the age groups 7-10 years and 15-18 years gave equal importance to two or more physical features, while those aged 11-14 years generally placed on different positions the investigated physical features.

For the children aged 7-10 years, their primary concern regarding their physical appearance is the eye colour, the graphic recording at this level a pronounced ascending line. The other physical characteristics record close values in the following descending order: weight and appearance of hair at the same level followed by height, and dental appearance, the least inquiring one.

Students aged 11-14 years show the most intense preoccupation for eye colour, followed by weight, height, hair appearance and the lowest concern for the dental appearance.

Hopefully, adolescents aged 15-18 years show the utmost importance for their dental appearance, followed in descending order by concerns for: hair appearance, height, weight, eye colour.

If we conduct a separate analysis by gender, we shall obtain different

results (fig. 2, fig. 3) in the sense that the concern for eye colour among girls aged 7-10 years is much higher than among boys of the same age and girls show more concern for their dental appearance compared to boys.

No high differences were recorded between the assessments made by girls aged 11-14 years compared to boys of the same category, but even here girls show more concern for their dental appearance compared to boys.

The category 15-18 years recorded differences by gender, meaning that boys are more concerned with their dental appearance and height than girls, and girls are more interested in their eye colour.

At a closer investigation on how children and adolescents assess the importance of their dental appearance, it appears that those aged 7-10 years considered their dental appearance as the most important one, or on the 2nd place, while for most children aged 11-15 years their dental appearance was the least important one. High school students showed the highest concern for their dental appearance (fig. 4).

81.95% of the boys aged 7-10 years did not know that the doctor who aligns teeth is not the same doctor who treats teeth. 89.70% of the girls aged 7-10 years thought that the doctor who aligns teeth is not the same doctor

who treats teeth. Of the students aged 11-14 50.60% - boys and 46.42% - girls did not know that the doctor who aligns teeth is not the same doctor who treats teeth. Of the high school students, 76.27% of the boys and 33.33% of the girls did not know that the doctor who aligns teeth is not the same doctor who treats teeth. The first two age groups recorded minimal differences by gender, and the girls of the age group 15-18 years were better informed in this respect compared to boys (fig. 5).

80% of the children in age group 7-10 years believe that the doctor who aligns teeth is the dentist, 13.57% chose the orthodontist and 4.28% chose the family doctor, with minimal differences by gender. 43.97% of the students in secondary school consider that the dentist is the doctor who aligns teeth, 54.81% chose the orthodontist and 1.20% chose the family doctor. 38.93% of the high school students consider that the dentist is the doctor who aligns teeth, 60.17% know that it is the orthodontist the doctor who aligns teeth and 0.88% chose the family doctor. Girls of age groups 11-14 years and 15-18 years are much better informed about the existence of the orthodontist than boys of the same age are. There has been no confusion with the paediatrician at this question (fig. 6).

Most children and adolescents are aware of the fact that there are appliances for straightening teeth i.e. 92.50% of those aged 7-10 years, 95.18% of those aged 11-14 years and 92.03% of those aged 15-18 years. There were only boys from the category of high school students who did not know about the existence of orthodontic appliances (7.96%) (fig.7).

When asked "Would you wear an orthodontic appliance (to align your teeth)?" 51.42% of the primary school children would agree to wear one, 22.86% would not accept to wear one while the rest 25.71% answered "do not know". 55.72% of the secondary school

students would agree to wear one, 17.47% would not accept to wear one and 26.81% answered "do not know". 44.54% of the high school students would accept to wear one, 18.59% did not agree to wear one and 36.87% answered "do not know". One can notice that girls in each age group show more intense concern about wearing appliances than boys do (fig. 8).

Children aged 7-10 years believe that an appliance would bother them firstly while eating (57.85%), but also while speaking (34.28%) and less while smiling (29.28%). For those aged 11-14 years, both girls and boys consider that an appliance would bother them firstly when smiling (53.61%), but also when eating (45.18%) and speaking (31.32%). High school students considered to the highest percentage that an orthodontic appliance would bother them especially when smiling (52.21%), but also when speaking (34.51%) and only a few (25.66%) think that an orthodontic appliance would disturb them during the process of mastication (fig. 9).

Analyzing the answer to the question "Have you been told by parents or friends that your teeth are not aligned?" one can notice that the highest percentage (50.71%) of the children aged 7-10 years found out that they present certain dento-maxillary anomalies, 32.83% of those aged 11-14 years were informed about dento-maxillary anomalies, the lowest number of students who needed to be told about dento-maxillary anomalies (22.12%) were high school students. In all age groups the gender distribution regarding the answer to this question was almost equal (fig. 10). We believe that this result is related on one hand to the disorders caused by the eruption of the permanent teeth both in phase I and in phase II of mixed dentition and on the other hand to the fact that there are anomalies with a tendency of spontaneous improvement, and as growing old some children and

adolescents followed an orthodontic treatment to correct their dento-maxillary anomalies.

In a study conducted by Siegelman and Shaffer to assess the level of self-esteem at ages 8-11 years, 12-14 years and 15-18 years, the authors conclude that the biggest problems related to self-image appeared in the case of children aged 12-14 years, in the sense of low self-esteem. The explanation could be that at the age of 12-14 adolescents accumulate a number of physical changes for which they does not possess a satisfactory level of psychological knowledge. The body image, located on the edge of conscience in childhood, becomes central, embedding into self-consciousness. It is the period when adolescents spend more time in the bathroom, stare more in the mirror. The desire of correcting or masking various physical imperfections becomes more evident with girls. Both girls and boys are worried about acne, weight, wearing glasses, dento-maxillary disharmonies. [2]

It is unfortunate that little is known about the existence of possible treatments of the dento-maxillary anomalies, respectively about orthodontics, since early orthodontic intervention can reduce much the need for treatment in the second phase of the mixed dentition or permanent dentition. [3,4]

There are limitations of the methods of assessing patients' health awareness, treatment planning and assessment of therapeutic response in children. [5] On the other hand, there is a large set of patient-centred assessments in terms of life standard or life standard based on the condition of the oral health applied to the adult population in various countries and commonly used in epidemiological studies. [6,7,8] However, assessing the impact of oral health on the life standard in children is far more complex, not only because of the huge

psychosocial changes that occur during childhood, but also due to rapid changes in the evolution of their physical aspect. [9] Cognitive development of children varies greatly in terms of vocabulary and understanding the meaning of the items used by the psychological tools varies greatly even in children of similar ages. However, the changes that occur in children during their physical and mental development make it difficult to compare repeated measurements. [10]

Most orthodontist authors recommend the need for early detection of dento-maxillary anomalies, from the first phase of the mixed dentition, with the need for therapeutic measures to prevent the aggravation of the existing anomalies and to provide a favourable environment for the development of the jaw. This is possible only through public information, from a young age and by applying screening methods of diagnosis. [11,12,13,14,15]

Prevention in orthodontics and early treatment of the dento-maxillary anomalies are still much debated worldwide and are subject of controversy mainly for the cost-effectiveness ratio, in terms of patients' functional and psychosocial benefits. Many authors consider that the optimal time for treatment is the second phase of mixed dentition [13,16,17], but there are authors who prefer early orthodontic treatment (in the first phase of the mixed dentition) and insist on investigations regarding vicious habits, dysfunctions and parafunctions at the earliest age. [11,12,13,16,18,19]

Within inter-individual relations, people spend more time focusing on the aspect of their interlocutor's eyes and mouth and a less time on other facial features. A study showed that, for the general public, the aesthetics of the smile is ranked second after the eye aspect in the attraction expressed by people's physiognomy. [20]

Aesthetic standards regarding the smile aspect must take into account: a symmetrical smile, the lower lip parallel to the incisal edge of the upper front group and the gingival margin of the upper alveolar border visible on a portion of 0.1-1 mm, the golden ratio in terms of tooth size and the absence of the buccal corridor. [21,22,23,24] As far as the shape of teeth is concerned, women prefer more blunt teeth, while men prefer teeth with better defined angles. [25]

The size of the buccal corridor still remains a controversial aspect, defined as the space between the buccal surfaces of the maxillary molars and the labial angle while smiling. [26,27] Some authors use the inter-canine dimension to define the size of the buccal corridor. [28,29] Most

orthodontists consider the absence of the buccal corridor as more aesthetic than its presence during smiling, and in case of a buccal corridor, its size should be as small as possible. [31,32,33]

Perhaps the results obtained in the research would not be so surprising if we extended the study to the adult population because there were quite a lot of situations where the teachers we worked with during the study had no knowledge of the existence of orthodontics as a medical specialty, the term of orthodontic appliance being reduced to the meaning of "denture". Many of them reported that we should insist on proper psychological conditioning on parents as they have to explain children the necessity of following an orthodontic treatment.

## CONCLUSIONS

We found out that children and adolescents show increased interest in their physiognomy within their general body appearance. Children aged 7-14 years showed less preoccupations for their dental aspect while those aged 15-18 years showed more intense preoccupations for the same aspect.

There are several shortcomings and deficiencies of the educational

system regarding the importance of the orthodontic treatment. Thus, over 80% of the primary school children that I questioned did not make the difference between a dentist and an orthodontist. Almost 50% of the secondary and high school students did not make this difference.

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# CLASSIC VERSUS HYBRID DISJUNCTION THERAPY

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## ABSTRACT

*The classic disjunctur is composed out of 4 rings that are cemented on the first premolars and first maxillary molars, united by 4 bars and a median screw which is activated obtaining maxillary disjunction. This classic device has secondary side-effects after activation, including vestibular version of the anchorage teeth, open bite, etc. The hybrid disjunctur is a new device which uses skeletal as well as dental anchorage. This way, side effects are avoided.*

*The hybrid disjunctur is composed out of two rings on the molars, two palatal miniimplants in the front, united by a disjunction screw. This device can be used in lower ages, starting 7 years of age, as well as for older patients. Following this type of disjunction, the palatal suture opens parallel and the dental side-effects can be diminished or even absent.*

**Key words:** Skeletal anchorage, orthodontic mini-implants, disjunction

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## INTRODUCTION

The first steps in the disjunction therapy have been described by Angell E.C. in 1860, but in those times times disjunction could not be demonstrated radiologic.. Landsberger was the first to demonstrate it. Angle E.H and Hawley C.H weren't satisfied by the method and excluded it. It was introduced again during the mid last century through the contributions of Hass and Korkhaus, in 1958.

By classic disjunction, the transversal delay of the upper jaw can be corrected, but serious side-effects

can appear: vestibular version of the anchorage teeth, fenestrations of the vestibular plate showing vestibular roots, root resorption or gingival retractions. To avoid these problems, during the last years, disjunctors with completely skeletal anchorage have been introduced but they need surgical assistance.

Wilmes is the first author who describes a hibrid disjuncor, that uses both skeletal and dental anchorage, named Hybrid-Hyrax.

## MATERIAL AND METHOD

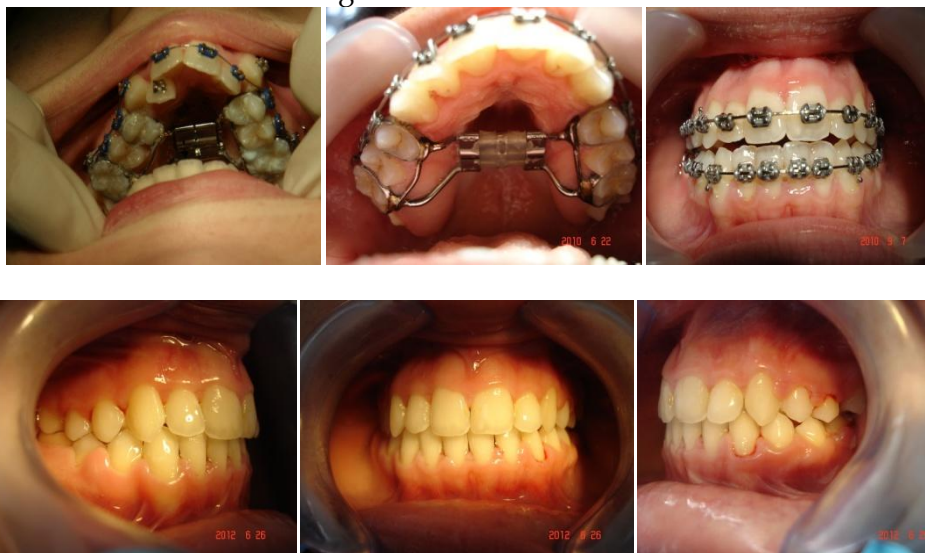
The classic disjuncor was applied in cases of dento-alveolar disarmony, with space deficit and transversal delay favouring the lower jaw. In literature, the limit for this procedure is 12-14 years.

The hibrid disjuncor allows the free treatment of the frontal part, accelerating the treatment. In the posterior part, the disjuncor is anchored by 4 cimented ringd on the first upper molars. In the frontal part, two 8 or 10 mm Tip Ortho Easy mini-implants are placed and united with the molars by the orthodontic screw. Miniimplants have a double function: assuring skeletal anchorage for the frontal area and not allowing the

vestibular basculation of the molars. Activation of the hybrid disjuncor is done by turning the activation key 180 once every day. It can be applied even in patients aged 17-20 years.

### Case 1

13 years old patient, with dento-alveolar disarmony, crowdings, multiple rotations and versions. Two classic disjunctors have been placed because the first one didn't achieve enough space to align the teeth. Fixed orthodontic treatment resulted in neutral occlusion following extraction of the four first molars (because after disjunction, an open bite appeared).





## Case 2

17 years old patient, prognatism and pronounced facial asymmetry, having multiple extraction in the upper jaw previous to the orthodontic treatment. The patient had a bilateral crossbite and vertical frontal occlusion. Using the hybrid disjunctor, an opening of 7 mm of the medio-sagittal junction was obtained though the patient was 17 - age where the classic disjunctor

would'nt have worked. At the same time the patients was wearing a Delaire mask with "elephant" elastics. The occlusal jumped was obtained, resulting a 4 mm sagittal step and frontal overbite. The mesialisation of the lateral group follows for both maxillary sides and implant treatment for the edentations.



## DISCUSSIONS

The advantage of this therapy is its applicability to all ages, especially in mixed dentition when premolars aren't erupted comparing it to the classic disjunctor where the eruption of the premolars is necessary. Another advantage is that during the treatment, the anterior arm of the disjunctor is free, compared to the classic one where it is blocked, resolving more issues at one time.

The hibrid disjunctor has applications for older ages, after puberty, having very good results in these cases.

The contention of the disjunctor is reduced to half comparing it to the classic one, meaning three months after finalizing the transversal expansion, when it can be removed from the molars and the mini-implants.

## CONCLUSIONS

After the eruption of the first molars, the hibrid disjunctor can be used, no matter if the other teeth are erupted. In case of the hibrid

disjunctor a parallel opening of the medio-sagittal junction is obtained, and the vestibular version of the anchored teeth is reduced to the

minimum. It is a relatively simple to apply method, without having any

secondary risks. The age limit for this device is 17-20 ani, maybe even higher.

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# INVESTIGATION OF WORKING POSTURE AMONG DENTAL LABORATORY TECHNICIANS



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## ABSTRACT

*Introduction: The goal of ergonomics is to establish a healthy working environment. The profession of dental technician often*

*implies a fixed working posture or repeated and precise force application, which stress the body.*

*Objectives: The study's objective was to examine the ergonomic posture of the dental technicians from Timisoara.*

*Material and Method: 20 dental technicians and 30 students at Faculty of Dental Medicine Timisoara- Dental Technology Specialization were taken into study. One used the questionnaire method to test the theoretical knowledge regarding the ergonomic aspects in the dental technology laboratory. Further, their working posture in the laboratory was investigated with help of the thermograph FLIR B200(FLIR SYSTEMS, Hong Kong), that belongs to Mechatronics Department of Politehnica University Timisoara.*

*Results: The thermograms present the areas subjected to extended muscle contraction (isometrical). The questionnaire revealed that 60% from dental technicians adopted a good working posture, beside only 35% from students. The most problems appeared at the proper adjustment of the stool at working table and the head tilting- more than 25°.*

*Conclusions: Both the dental technicians and the students may develop muscle-skeletal disorders, because of their bad working posture. The identification and correction of postural inaccuracy may prevent/minimise the negative consequences.*

*Key words: dental technician, thermograph, ergonomics*

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## INTRODUCTION

The profession of dental technician requires repeated and precise force applications, frequently demanding a fixed posture that can create occupational hazard. In addition, technological advances have led to an increased workload among the dental technicians, which also impacts occupational risks. Although such technologies can simplify the work, they frequently ignore the role of posture in daily work. This negligence is reflected in the growing number of complaints specifically related to work-related muscle-skeletal disorders - WMSDs [1].

For example, 55.4-93% of dental professionals (dentists, dental hygienists and dental technicians) experience WMSDs, with the highest risk in elderly subjects and women. Spine, shoulders, elbows and hands are the most likely areas of the body to be involved [2].

The improper organization of the working space forces the dental technician to take many painful

working positions. They put pressure on nerves and blood vessels, causing elongation/excessive effort in the muscles, reducing circulation and further wear on the joint structures [3].

Ergonomics is defined as a set of multidisciplinary knowledge applied to the organisation of labour activities and elements to make up a job. The goal of ergonomics is to establish a safe, healthy and comfortable working environment, thereby preventing health problems and improving productivity [4].

The identification and correction of postural inadequacies may help prevent or minimise the consequences of labour practises 5,6. In this purpose, the literature recommends different tests for evaluation.

### OBJECTIVES

The objective of the present paper was to examine the ergonomic posture of the current and future dental technicians from Timisoara and to give advice about the right working posture.

## MATERIAL AND METHOD

20 dental technicians and 30 students at Faculty of dental Medicine Timisoara- Department of Dental Technology were taken into study (with their informed consent).

In the beginning one used the questionnaire method to test their theoretical knowledge regarding the ergonomic aspects in the dental technology laboratory. We identified in the literature eight principles regarding ergonomic posture in the field of dental technology, namely:

1. The angle between the lower and upper leg, with the legs slightly spread, must be  $\sim 110^\circ$  or slightly more;

2. The dental technician should sit symmetrically and as far back as possible in the seat, tilting the

upper body forward to a maximum of  $10-20^\circ$ , avoiding rotation and lateral slopes;

3. The head can be tilted forward to up to  $25^\circ$ ;

4. The pedal must be positioned close to one of the feet;

5. The upper limbs should be in front of the trunk, with the forearm raised from  $\sim 10^\circ$  to a maximum of  $25^\circ$ ;

6. The working field must remain aligned with the front of the upper body, with a distance between the working area and the eyes (or glasses) of  $\sim 30-40\text{cm}$ ;

7. The hand tools should be positioned within the visual field of the dental technician at a distance of  $20-25\text{cm}$ ;

8. The operating light should be positioned so that the light beam is running parallel to the viewing direction.

Data were analyzed by descriptive statistics.

Further, the working posture of the same dental technicians and students in the laboratory was checked and photographed in infrared with

help of a thermograph, namely the thermograph FLIR B200 (FLIR SYSTEMS, Hong Kong), that belongs to Mechatronics Department of Politehnica University Timișoara. Photographs/thermograms were taken casually and not necessarily on the same day.



Fig.1 . The thermograph FLIR B200 (FLIR SYSTEMS, Hong Kong)

## RESULTS

The results of the present study indicate a lack of adequate posture by the investigated dental technicians and students, during work, despite the laid-down teaching effort, regarding labour protection and ergonomics principles.

The photographs/thermograms revealed that 60% from dental technicians adopted a good working posture, beside only 35% from students. From among the eight principles that define the ergonomic

posture, the most problems appeared at the proper adjustment of the stool and the head tilting- more than 25°.

Although 65% from the students had theoretical knowledge, only 35% from them worked in accordance with the ergonomic principles regarding the working posture.

Table 1 presents the theoretical knowledge and the proper practical application of each ergonomic principle.

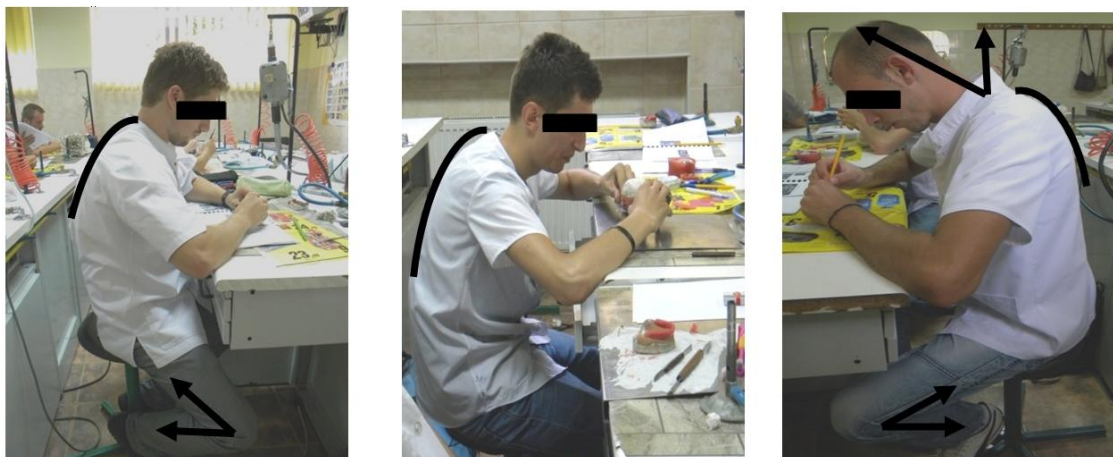


Fig.2. Different working positions of the students, that indicate an unhealthy working posture.



Tab. 1. The theoretical knowledge and the proper practical application of each ergonomic principle-student/ dental technician

Requirements	Theoretical knowledge % Student / Dental technician	Practical application % Student / Dental technician
The angle between the lower and upper leg, with the legs slightly spread, must be $\sim 110^\circ$ or slightly more- proper stool adjustment.	50/ 60	30/ 48
The dental technician should sit symmetrically and as far back as possible in the seat, tilting the upper body forward to a maximum of $10\text{-}20^\circ$ , avoiding rotation and lateral slopes.	68/ 65	37/55
The head can be tilted forward to up to $25^\circ$ .	47/ 55	33/ 45
The pedal must be positioned close to one of the feet	81/ 95	51/ 72
The upper limbs should be in front of the trunk, with the forearm raised from $\sim 10^\circ$ to a maximum of $25^\circ$ .	61/ 58	42/ 58
The working field must remain aligned with the front of the upper body, with a distance between the working area and the eyes (or glasses) of $\sim 30\text{-}40\text{cm}$ .	73/ 85	41/ 72
The hand tools should be positioned within the visual field of the dental technician at a distance of $20\text{-}25\text{cm}$ .	74/ 80	30/ 67
The operating light should be positioned so that the light beam is running parallel to the viewing direction.	53/ 65	33/ 63

The photographs/thermograms present the areas subjected to extended muscle contraction (isometrical). The red surfaces represent the areas with high values of temperature (intense

muscle activity), while the yellow, green and blue surfaces represent the areas with lower temperature (poor muscle activity) (Fig.3).





Fig. 3. Aspects of different working position – dental technicians and students (a,b,c,d- photography/ a',b',c',d'- thermogram).

## CONCLUSIONS

Posture reflects the position that a person maintains in space through his bone-muscle-skeletal system, according to a static and dynamic balance. By maintaining a good posture, the body lowers its energy expenditure, improves organ functioning and is protected against disturbances that could undermine occupational practice.

The ergonomic posturing of the surveyed dental technicians and students was not appropriate. This indicates the fact that, they may develop WMSDs. The WMSDs to which the dental technician is most exposed would be the upper extremity muscle-skeletal disorders- cervical

spondylosis, tension neck syndrome. Chronic tendinitis is also frequent especially at senior practitioners, as result of the work with vibrating tools. The highest attention should be paid on practical implementation of ergonomic principles in the field of dental technology (the sooner the better), in order to prevent or delay the WMSDs [7,8].

It is necessary to investigate how to improve the learning process of proper posturing. The didactic use of digital images may have an influence in understanding this.

### Acknowledgements

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# CLINICAL ASSESMENT OF DIFFERENT METHODS USED FOR PROFESSIONAL DENTAL HYGIENE



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## ABSTRACT

*Objective.* The aim of this study is to compare different methods used in dental hygiene including Prophylflex and conventional methods such as manual scaling, ultrasonic scaling and professional tooth brushing.

*Materials and methods.* 94 patients, divided in 3 groups were included in a preventive program for a 2 years period, applying to each group one professional hygiene method every 3 months. The following indices: Oral Calculus Index (OCI), plaque index Quigley-Hein modified by Turesky (QH) and the gingival index Loe and Silness (GI) were used to evaluate the efficiency of each method.

*Conclusion.* The results indicate that Prophylflex is a good alternative to conventional methods of professional dental hygiene.

**Key words:** plaque control, scaling, modern prophylaxis, Prophylflex

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There is no universal or simple way to define what is "health" and what is "disease". Indeed, these very notions may differ according to regions, populations or age categories in the world. Furthermore, our perception of health and disease has changed over the years. Health was previously defined as a "state of physical, mental and social wellbeing and ability to function and not merely the absence of illness or infirmity". Today, health is a relative entity and a healthy person is someone who is able to lead an economically and socially productive life (WHO 2005).

Oral health certainly fits within the broader domain of health related quality of life. Quality of life has been profoundly influenced by modern economic development (Feinstein 1993, Govaerts 1995). This applies particularly to industrialized countries where the quality of life of populations is part of economic values and has reached high standards (Diderichsen 1990, Scheuch, 1995). The oral health of a population is influenced by many parameters, including exposure to risk factors, susceptibility to disease and psychosocial and behavioral factors.

Throughout life, all external surfaces of the body are exposed to colonization by a wide range of microorganisms. In general, the establishing microbial flora lives in harmony with the host. Constant renewal of the surfaces by shedding prevents the accumulation of large masses of microorganisms. In the mouth, however, teeth, implants and prosthetic devices provide hard, non-shedding surfaces for the development of extensive bacterial deposits.

It is well documented that tooth brushing and other oral hygiene procedure can prevent or control gingivitis and periodontal diseases. The control of dental plaque is the key factor in preventing gingivitis, periodontal disease and dental decay.

It is linked directly to the only etiological factor of these diseases: oral pathogenic bacteria which colonize the dental surfaces and forms the dental plaque.

Mechanical plaque control by professional tooth cleaning involves removal of supragingival plaque and 1-3 mm of subgingival plaque with the use of a mechanically driven instrument and prophylaxis paste. It may also include the removal of calculus and deep subgingival plaque.

Hygiene in dentistry has reached today new shapes and dimensions. A delicate issue like the removing of dental plaque, of soft deposits and smoke and coffee discolorations it could be solved with the help of modern methods of professional hygiene.

Modern prophylaxis admits the importance of clean dental surfaces and it was born from the necessity of obtaining good results in removing dental plaque and discoloration.

In clinical practice there are frequently situations in which after classic therapeutic measures including manual scaling and ultrasonic scaling, dental surfaces or restorations showed fine dental plaque tracks or calculus deposits.

That is the reason why Prohyflex became so important in every day practice. Prophyflex incorporate a unique system of cleaning different from other systems which are pulverizing separately the water and the air / abrasive particles. Prophyflex releases a homogeneous water-air-bicarbonate of potassium mixture at the tip of the hand piece just before the emission of the stream.

This thing provides the rounding of the crystals of bicarbonate, the mixture being abrasive and also having a gentle action on the dental surfaces and implants of titan on which they didn't determinate rough surfaces. (Barnes et.al.1994).

The dental plaque grows more rapidly on titanium than on the enamel; that is why the patients with are having problems on implants needed more often dental check-ups for hygiene, achieved in the present time much easier and much faster with the help of Prophyflex.

Comparative with the dental hygiene units that are existing on the

market in this moment, Prophyflex utilizes this homogeneous mixture which can get access in places which are not accessible to usual cleaning systems like the interproximal areas, the spaces between brackets and orthodontic ring- without showing losses of composite or cement because of the diffusion of the stream around of this elements.

## MATERIAL AND METHOD

The study was performed at the Department of Preventive, Community and Oral Health after obtaining the approval from the Ethical Committee of the University of Medicine and Pharmacy Timisoara and the written consent from the patients included in the study. From 135 patients with age between 18-45, for this study were selected 94 patients with calculus deposits and pigmentation of the dental surfaces. The study was developed over a two years period (2010-2012) and the patients were recalled every 3 months. They were included in a preventive program (prophylactic measures including oral hygiene instruction and demonstration

of oral hygiene techniques using disclosing solutions, professional cleaning of all tooth surfaces and topical application of fluoride).

Prophylaxis had also with emphasis on interproximal cleaning and professional mechanical plaque control including scaling and polishing with abrasive pastes as classic preventive measures and the use of Prophyflex as a modern alternative in prophylaxis.

The patients were divided in 3 groups according to the quantity of the calculus deposits evaluated in the first clinical examination by using oral calculus index (OCI).

The Oral Calculus Index (OCI, Greene & Vermillion 1960, 1964) scores are assigned according to the following criteria:

- 0- no calculus present
- 1- supragingival calculus covering not more than one-third of the exposed tooth surface being examined
- 2- supragingival calculus covering more than one-third but not more than two-thirds of the exposed tooth surface, or the presence of individual flecks of subgingival calculus around the cervical portion of the tooth
- 3- supragingival calculus covering more than two-third of the exposed tooth surface, or a continuous heavy bank of subgingival calculus around the cervical portion of the tooth

Patients were divided into 3 groups, according to the OCI index, as follows:

Group	Number of patients	OCI
1	25	2,1-2,4
2	37	1,2-1,8
3	32	0,4-0,8

In the first appointment without taking in consideration the professional

hygiene method applied, there were filled the dental files to all of the

patients, registering the dental plaque and gingival indices.

In order to reveal the dental plaque it was used as disclosing agent the Plak -Lite system a more efficient method for observing the dental plaque deposits with the help of a light

source which disclose the dental plaque in yellow.

Plaque was assessed by the Turesky-Gilmore-Glickman modification of the Quigley and Hein plaque index (QH).

The Turesky modification of the Quigley Hein plaque index scale (Turesky et al,1970)	
0 =	No plaque/debris
1 =	Separate flecks of plaque at the cervical margin of the tooth
2 =	A thin continuous band of plaque (up to 1mm) at the cervical margin of the tooth
3 =	A band of plaque wider than 1mm but covering less than 1/3 of the crown of the teeth
4 =	Plaque covering at least 1/3 but less than 2/3 of the crown of the tooth
5 =	Plaque covering 2/3 or more of the crown of the tooth

For evaluating the status of the gingival tissue it was used the gingival index Loe and Silness (GI).

The Gingival index (GI) of Loe and Silness	
0=	Normal gingiva
1=	Mild inflammation-slight change in color, slight edema
2=	Moderate inflammation-redness, edema and glazing. Bleeding on probing
3=	Severe inflammation-marked redness and edema. Ulceration. Tendency toward spontaneous

Scaling is the basic procedure by which calculus is removed from the surface of the teeth. Scaling is divided into supragingival and subgingival scaling, depending on the location of

the calculus in relation to the gingival margin. For the supragingival scaling it was been used scalers: sickle, hoe and chisel.

## RESULTS

To the first group formed by 25 patients with massive calculus deposits it was proceeded manual scaling and professional tooth brushing with abrasive pastes and after that it was used again a disclosing agent and we recorded the new value of the dental plaque index (table1).

For the second group it was performed professional cleaning by using ultrasonic scaling, followed up by professional tooth brushing and the determination of the new dental plaque indices (table 3).

Table 1. Quigley-Hein indices modified by Turesky before and after manual scaling

Group 1	Number of patients	OH indices
BEFORE	14	4,2-4,8
	11	3,3-3,7
AFTER	19	2,4-2,9
	6	1,7-1,9

Table 2. The values of the gingival indices before and after manual scaling

Group 1	Number of patients	GI indices
BEFORE	17	1,8-2,3
	8	0,7-1,5
AFTER	14	1,3-1,8
	11	0,6-0,9

Table 3. Quigley-Hein indices modified by Turesky before and after ultrasonic scaling

Group 2	Number of patients	OH indices
BEFORE	29	3,8-4,4
	11	2,8-3,5
AFTER	31	2,1-2,3
	6	1,2-1,6

Table 4. The values of the GI indices for the second group before and after ultrasonic scaling

Group 2	Number of patients	GI indices
BEFORE	20	1,4-1,7
	17	0,9-1,2
AFTER	12	1,1-1,3
	25	0,4-0,6

The third group was formed by 32 patients and they were cleaned with the help of Prophyflex.

The scores before and after the cleaning were:

Group 3	Number of patients	OH indices
BEFORE	18	2,5-2,8
	14	1,7-2,1
AFTER	12	0,8-1,2
	20	0,4-0,6

The patients were recalled every 3 months for a period of two years. To every 3 months we proceeded to the evaluation of dental plaque indices and gingival indices and it was also initiated a cleaning program individualized to each patient in accordance to its personal needs for treatment. For that, conventional methods consisting of manual scaling, ultrasonic scaling were combined with professional tooth cleaning using Prophyflex.

In the second part of the study it was also applied to the first and to the second group professional cleaning with Prophyflex. The results obtained were similar to the results that were obtained to the third group: score 0 at the dental plaque index. Obviously the maintenance of these results is related to each individual personnel skills and ability to practice every day proper dental care.

## DISCUSSIONS

The first objective of treatment is to create an environment in which the tissues can return to health. In the sequence of patient treatment, introduction to preventive measures is first, before professional instrumentation. After health has been attained, the patient's self-care on a daily basis is essential to keep the teeth and gingival tissues free from disease caused by the microorganism of bacterial plaque. Professional instrumentation makes a limited

contribution to arresting the progression of disease without daily plaque control measures by the patient.

General objectives are that dental hygiene instrumentation will: create an environment in which the tissues can return to health and then be maintained in health, aid in the prevention and control of gingival and periodontal diseases by removal of factors that predispose to the retention of bacterial plaque (dental calculus, irregular and overhanging

restorations), provide the patient with smooth surfaces which are easier to clean and to keep plaque free.

After 2 years of study the results indicated that there was a good improvement in the oral health of the patients but with regard to the effectiveness of instrumentation it was apparent that there was little difference in clinical response between manual, ultrasonic instrumentation and the use of Prophyflex.

The evaluation of dental plaque accumulation by using QH indices showed that the dental surfaces were much cleaner and the rate of the accumulation is significantly lower to third group cleaned with Prophyflex even in the absence of properly dental care (regularly oral hygiene habits, dietary control). The results indicated that in the case of using Prophyflex the surfaces were much easier to maintain clean - a smooth surface is easier for the patient to keep clean.

Removal of subsequent calculus deposits is easier because calculus will be less firmly attached to a smooth surface than to a rough one in which the calculus could become embedded in undercuts and other tooth surface irregularities.

The evaluation of the results indicated that for the patients that was applied manual scaling and ultrasonic scaling the results obtained were definitely improved, but it could not be comparable with the results obtained by using Prophyflex.

The quantification of the results was made by following the values of

the dental plaque and gingival indices before and after applying dental hygiene measures. The variation between the 3 groups was due to the hygiene habits of the patients and the inconstant self-performed tooth brushing.

The third group had the best results with a tendency to completely reduce the dental plaque accumulation.

The efficiency of the Prophyflex system derives from the numerous advantages when it is compared with conventional methods: it is pain-free, it does not have negative effects on the human body, it does not need special installation (it uses a low pressure 35psi-it permits the adaptation to the dental unit in the place of the turbine), it is small, portable, easy to use, the hand piece is removable, easy to clean, it could be used for bleaching of tooth, it is an alternative to the scaling of the teeth with high sensitive and the time for work is reduce to half.

When dental probe was used to the first two groups were detected roughish surfaces (it was a sign that the dental surface was not properly cleaned existing the risk of the reconstruction of the calculus deposits and dental plaque deposits). In the case of using Prophyflex all this inconvenience does not exist. Dental surfaces were clean, smooth, bright to the patients that had professional tooth cleaning with t Prophyflex in stead of the patients which were cleaned by using conventional methods.

## CONCLUSIONS

The use of Prophyflex increased effectiveness of plaque control measures. The use of the Prohyflex is a good alternative for obtaining aesthetic results, but in the case of massive

calculus deposits the therapeutic measures are oriented on using manual scaling, ultrasonic scaling and professional cleaning.

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# ORAL HEALTHCARE OF PRESCHOOL CHILDREN – STUDY OF PARENTS' KNOWLEDGE



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## ABSTRACT

**INTRODUCTION:** Educational models provided by parents have a decisive significance in shaping the child's oral health behavior.

**METHOD:** A cross-sectional study was conducted during 2010-2012. A self-administered anonymous questionnaire was distributed among 460 parents with preschool children.

**RESULTS:** Most respondents were females (88%), the majority (61.4%) had education higher than secondary school level and the main source of information was the dentist. Regarding methods of preventing caries, less than one third choose regular tooth brushing, 19.5% dental check-ups and 10.7% sealing teeth. In terms of knowledge about the erupting age of first permanent molar, half of parents answered correctly and 46.3% knew that it appears behind the temporary molars. **Conclusion:** The relatively low level of parental knowledge indicated a need for dissemination of information about factors influencing the oral dental care of preschool children and oral health promotion in kindergartens.

**Key words:** education, parents, preventive care, preschool children

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## INTRODUCTION

Educational and cultural models provided by parents have a decisive significance in shaping the child's oral health behavior [1]. It is very important for parents to understand that they are examples for their children. Ideally, parents education should take place simultaneously with the child; in this way, parents can learn how to improve their own oral hygiene and, at the same time, to be able to assist the child while performing daily oral hygiene and to promote a health oral health behavior [2].

### OBJECTIVE

The study aims to assess parents' knowledge on the first permanent molar, given that often it is considered a temporary tooth, the early lesions are ignored and children come late to the dentist for oral health care. Given the serious repercussions that can occur in the absence of timely establishment of preventive or curative treatment, we want to draw attention to the need of informing parents about the impacts on dental-maxillary system and about the motivation for regular check-ups and reducing the child exposure to behavioral risk factors for oral health.

## MATERIAL AND METHOD

It was used a self-administered anonymous questionnaire recommended by the World Health Organization. In the study were invited to participate, 460 parents of preschool children from four kindergartens in Bucharest, chosen randomly, in 2010-2012. At first, parents were informed about the purpose of the study and data confidentiality. Afterwards, has been obtained the informed consent from kindergartens managers and parents. Finally, 410 parents returned the completed questionnaire, the responsiveness rate being 89.1%. The

questionnaire contains knowledge items related to methods for preventing dental caries, first permanent molar (eruption age and place,) and demographics data of the respondents. Parents were explained the purpose of the study and were assured of confidentiality. Interpretation of data obtained from responses to the questionnaire were analyzed using specialized software STATA 11C (StataCorp LP, Texas, USA, version 2009) and was performed a descriptive statistics.

## RESULTS

Characteristics of the study group  
Among all 410 subjects, most of them (75.8%) are aged between 26 and 35 years and the majority is female (88%). Epidemiological studies published in recent years have shown that there is a polarization of dental caries, especially due to socio-economic differences between different classes of the community<sup>1</sup>. These differences lead to inequalities in oral and general health. Therefore, we were interested

in the education level of parents. Out of the 410 parents, 64% (n = 262) had higher education, 6.8% (n = 28) post-secondary education and 29.2% (n = 120) with high school studies.

### Parental oral health knowledge

From all methods of prevention of dental caries, less than one third (28.7%) chose personal tooth brushing, 19.5% mention regular medical control and only 10.7% chose the sealing (Table I).

Table I. Parents' knowledge on methods of prevention of dental caries

Caries prevention methods	%	n		
	Total	Total	♀	♂
Personal brushing twice a day	28.7	118	106	12
Follow-up	19.5	80	70	10
Low sweet consumption	15.8	65	57	8
Sealing teeth	10.7	44	40	4
Use of fluoride tables	7.1	29	28	1

Regarding parents' knowledge about the eruption age of the first permanent tooth, 50% (n = 205) answered correctly, 25.3% (n = 104) incorrectly, and 24.7% (n = 101) admit they do not know. 46.3% (n = 190) of parents know that it appears behind molars, without replacing a temporary tooth, 22.5% (n = 92) said they did not know, and 31.2% (n = 128) responded incorrectly.

The last question concerns the sources of information of parents regarding oral health of their children (Table II). For most parents (39.1%) the dentist is the primary source of information. A percentage of 28.8% of respondents stated that they had not received such information, but there are parents who inform the mass media.

Table II. Information sources of parents on children's oral health

Sources of oral health information	%	n		
	Total	Total	♀	♂
Dentist	39.1	160	145	15
Magazines	15.3	63	57	6
Books	13.6	56	48	8
Pediatrician	2.7	11	9	2
Television	2.7	11	7	4
Teachers	1.5	6	5	1
None	28.8	118	78	40

## DISCUSSIONS

The results are broadly similar to other studies in our country: national study<sup>3</sup>, local –Bucharest<sup>4, 5</sup> and Timisoara<sup>6</sup> or abroad<sup>7, 8</sup>. It should be noted the increased number of parents who recognize that they have no information on the oral health of their children. Also, most parents are not aware of negative implications of sweets consumption and the importance of sealing or regular dental check-ups.

It should be noted that the analyzed group was not representative, especially by number, but also by the level of education of the parents, which in 64% of cases have higher education.

Even if, it is a well-known fact that even some educated adults have basic knowledge about oral health and many parents do not know how to help their children because they do not know how to do either for themselves.

It would have been desirable to correlate the results obtained from completing questionnaires with parents and children oral health status. Therefore, in a future study we intend oral clinical examination of parents and their children in our country to compare the results with data from literature.

## CONCLUSIONS

Our study results show a relatively low level of knowledge and low awareness of parents on preventive methods, requiring the need for health education on factors influencing oral health of preschool children.

Efforts are needed to raise parents' awareness about the importance of preventing diseases on temporary teeth and for increased addressability in dental offices for

prophylactic treatments or curative methods in the early stages of oral diseases.

Dentists, nurses, dental hygienist and dental students can and should play a major role in oral health promotion to preschool children, their parents and educators, too.

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# THE COST-EFFECTIVENES ANALYSIS OF PERINDOPRIL VERSUS CANDESARTAN CILEXETIL TREATMENT IN HYPERTENSIVE PATIENTS WITH LEFT VENTRICULAR HYPERTROPHY



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## ABSTRACT

*Aim and objectives:* The aim of the paper is to demonstrate the efficacy and costs for two antihypertensive regimens containing a converting enzyme inhibitor: perindopril and an angiotensin II receptor antagonist: candesartan.

*Material and methods:* The study included 189 patients: 110 received perindopril and 79 received candesartan. The efficacy is evaluated by reduction of blood pressure values and by improvement of parameters that characterize ventricular hypertrophy and diastolic function. The costs with medication and medical procedures were calculated according to the prices from Canamed 2013 and by those reimbursed by National Health Insurance Company.

*Results:* It has not been noticed a statistical significantly difference between the two therapeutic schemes regarding efficacy, but the cost of perindopril is lower than of candesartan.

*Conclusions:* The first therapeutic choice for a hypertensive patient with left ventricular hypertrophy could be perindopril because it is efficient and affordable. If the patient develops side effects the medicine will be change with candesartan.

**Key words:** perindopril, candesartan cilexetil, effectiveness, left ventricular hypertrophy, diastolic dysfunction, costs

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According to the Framingham study [7], hypertension is the cause of a quarter of heart failure cases. The guidelines for the diagnosis and management of heart failure evaluate that 70% of heart failure cases are due to the arterial hypertension [21]. For the hypertensive patients, the risk to develop heart failure is twice higher in men and three times higher in women. Very high and uncontrolled levels of blood pressure lead to pathological remodeling on the structure of the myocardial cell.

Except age, for hypertensive patients, left ventricular hypertrophy (LVH) is the most powerful predictor of cardiovascular complications (hypertensive cardiomyopathy, myocardial infarction, heart failure). Whether it is detected by electrocardiography, echocardiography or by MRI techniques, left ventricular hypertrophy is considered an independent risk factor for coronary artery disease, sudden death, heart failure or stroke. LVH involves changes in myocardial tissue architecture consisting of myocardial fibrosis and medial thickening of myocardial coronary arteries in addition to myocyte hypertrophy. [8]

Diastolic dysfunction is characterized by abnormalities in left ventricle distensibility, filling or relaxation and is the hemodynamic hallmark for hypertensive heart disease. The reduction of diastolic distensibility and impaired relaxation represent a pathophysiological link between hypertension and heart failure with normal ejection fraction. [20]

Diastolic dysfunction may be symptomatic or asymptomatic, it may occur to the hypertensive patients with or without LVH and it has an unfavorable prognostic. [8]

Studies that used Doppler echocardiography reported that approximately 20% of untreated patients with borderline or mild

hypertension have diastolic filling abnormalities in the absence of HVS. [8]

The proper treatment of hypertension provides a real benefit not only by improving it, but also by preventing, or by reducing the intermediate end-points which characterize the hypertensive disease: HVS and diastolic dysfunction.

Multicenter studies, including a large number of patients, showed a similar efficacy of different classes of antihypertensive medicines administered as monotherapy, or as a combined therapy on blood pressure. Although, their efficacy regarding the changes on the target organs is different. [11, 18]

The suppression of the renin-angiotensin-aldosterone system (RAAS) was found to offer a real benefit besides lowering blood pressure. It improves structural pathological changes of the heart. Therefore, the inhibitors of RAAS have multiple therapeutic indications in the cardiovascular pathology: arterial hypertension, post-myocardial infarction, heart failure. [8, 20]

Meta-analyses have shown that drugs which inhibit this system are associated with a significant regression of the left ventricular hypertrophy compared with other classes of antihypertensive drugs (beta-blockers, diuretics, calcium channel blockers). Studies have demonstrated their effectiveness also in improving left ventricular dysfunction (CHARM, PRESERVE, LIFE study). [3, 13, 23]

The effects of RAAS inhibition are due to hemodynamic mechanisms (reduction of blood pressure, decrease afterload), but also to load independent mechanisms related to the effects of angiotensin II, aldosterone and bradykinins on cardiac cells (reduction of myocyte hypertrophy, reduction in cardiac extracellular collagen matrix formation). [14]

The classes which are now the most prescribed are: converting enzyme inhibitors and angiotensin II subtype AT1 receptors antagonists.

Their effects on ventricular hypertrophy and diastolic dysfunction determine a significant reduction of hospitalizations due to symptoms of heart failure, reduction on cardiovascular morbidity and mortality and therefore lowered costs.

#### AIM OF THE STUDY

The study evaluated the efficacy and the costs of two therapeutic therapies: with perindopril and candesartan cilexetil. The efficacy was evaluated by blood pressure reduction and by modifications on parameters which characterize the ventricular hypertrophy and diastolic dysfunction of the patients. The costs are estimated by the price of medications, medical investigations and blood samples analyses.

### MATERIAL AND METHOD

The study group included 189 patients. They were hospitalized for one day at the Cardiology Clinic ASCAR from Timișoara. They were randomly assigned to receive either an converting enzyme inhibitor: perindopril (110 patients), or an angiotensin receptor blocker: candesartan cilexetil (79 patients). Patients in both groups also received concurrently, other antihypertensive agents to reach the blood pressure targets. The therapeutic scheme also included a lipid lowering agent (a statin).

The patients who presented: cardiac rhythm disturbances (atrial fibrillation), an ejection fraction lower than 50%, heart failure NYHA II, III, IV, high level of serum creatinine or myocardial infarction were excluded from the study.

The study was retrospective. It was performed during september 2012 – february 2013.

The patients received a therapeutic regimen regarding the stage of hypertension and the associated comorbidities. It included an inhibitor of renin-angiotensin-aldosterone system blocker and also other antihypertensive agents if the blood pressure was not well controlled: a beta-blocker, a diuretic and a calcium channel blocker.

The blood pressure target was 130/80mmHg in order to include also the patients with diabetes mellitus.

The blood pressure was measured at the beginning of the study and after 6 month with an sphygmomanometer. There were three consecutive readings. The echocardiographic assessment was made in the same time interval by a two-dimensional guided M- mode echocardiograph (GE Vivid PW/CW Doppler type).

The costs were calculated after Canamed 2013 prices for medicines. For medical consultation, medical procedures and laboratory data, the prices are those subsidized by the National Insurance Company.

#### Statistical evaluation

Data distribution was assessed by the Kolmogorov-Smirnov test. Continuous data were expressed as mean  $\pm$  standard deviation (SD). Categorical variables were represented as frequency and percentage. The statistical analysis of each parameter was assessed by Student's t test or Mann-Whitney U test, as appropriate. For the correlation analysis, Spearman or Pearson test was applied, depending on the Gaussian distribution. The level of statistical significance was established at  $p < 0.05$ .

## RESULTS

### A. The baseline demographic characteristics are shown in table1.

The baseline clinical characteristics did not significantly differ between the two groups of patients regarding age, the number of smoker patients, alcohol consumers or with diabetes mellitus.

A percent of 64.55% of patients treated with candesartan and 85.45% patients treated with perindopril had hypertension stage I or II. Many risk factors (smoking, obesity, diabetes

mellitus, hypertensive cardiomyopathy) associated with high blood pressure values were identified on a large percentage of patients in both groups. Therefore, a 58.18% of patients from perindopril group and 77.21% of patients from candesartan group were indentified as having a high or very high cardiovascular risk. Overall, of both groups, 63 patients (33.33%) were diagnosed with hypertensive cardiomyopathy.

Table 1. Initial demographic characteristics of the study patients

No.	Demographic characteristics	Patients treated with perindopril (n=110)	Patients treated with candesartan cilexetil (n=79)	p
1.	Age (years) (mean±SD)	59.23±11.18	56.42±14.19	0.1 <sup>†</sup>
2.	Female/male (no)	59/51	46/33	0.5 <sup>‡</sup>
3.	Smoker (no)	11	7	1.0 <sup>‡</sup>
4.	Alcohol consumers (no)	44	37	0.3 <sup>‡</sup>
5.	Low-salt diet (no)	6	8	0.2 <sup>‡</sup>
6.	Diabetic patients	28	22	0.7 <sup>‡</sup>
7.	Systolic BP/Diastolic BP* initial value (mean±DS)	152.74±11.99/90.68±8.55	147.30±25.12/91.08±12.86	0.1 <sup>†</sup>
8.	Cardiovascular risk: medium/high/very high (no)	23/40/24	13/19/42	0.0008 <sup>#</sup>

\*Systolic blood pressure/Diastolic blood pressure

<sup>†</sup> Student's *t* test

<sup>‡</sup> Fisher's exact test

<sup>#</sup>  $\chi^2$  test

### B. Initial biochemical characteristics of study patients

The patients of the two study groups presented the following initial values on the biochemical tests (table 2).

The patients of the two groups had similar mean values of cholesterol, cholesterol fractions (HDL-C, LDL-C), tryglicerides, serum ions, serum creatinine.

A low value of LDL-C/HDL-C ratio in 50% of the patients of both groups was noticed, it means that only a very few patients follow a diet or take a specific medication (for example

statins) to reduce this cardiovascular risk factor.

The incidence of high glucose serum values in the study groups was as follows: 34.17% of patients treated with perindopril and 30.90% of patients treated with candesartan cilexetil. These high incidence indicated an insufficient blood sugar monitoring or the development of de novo diabetes cases.

Patients did not present modified values of serum creatinine, the presence of renal impairment being an exclusion criteria from the study.

The serum ions were in normal ranges and similar for the both groups of study patients.

Table 2. Initial biochemical characteristics of the patients studied

No.	Laboratory values (mean±SD)	Patients treated with perindopril	Patients treated with candesartan cilexetil	p
1.	Total cholesterol (mg/dl)	202.94±46.22	207.28±40.79	0.5
2.	TG (mg/dl)*	144.83±69.55	133.85±61.69	0.2
3.	HDL-C (mg/dl)*	47.41±12.85	46.53±11.44	0.6
4.	LDL-C (mg/dl)*	125.59±37.97	131.68±36.86	0.3
5.	Serum creatinin (mg/dl)	0.86±0.19	0.85±0.19	0.6
6.	Potassium (mmol/l)	4.10±0.31	4.13±0.48	0.5
7.	Sodium (mmol/l)	140.34±4.19	138.45±4.14	0.0023
8.	Chlorine (mmol/l)	101.83±3.80	102.60±2.97	0.1
9.	Serum glucose a jeun (mg/dl)	108.68±32.67	116.9±46.59	0.2

\*HDL-C (high density lipoprotein cholesterol); LDL-C (low density lipoprotein cholesterol); TG (triglycerides)

### C. Evaluation of regimens efficacy

Regarding blood pressure values and the cardiovascular risk, patients were administered one, two, three or even four antihypertensive medicines. A very high percent of patients of both groups had three medicines in the

therapeutic scheme: 88 (80%) patients of those treated with perindopril as main drug and 59 (74.68%) patients of those treated with candesartan cilexetil, as it has been shown in the figure 1.

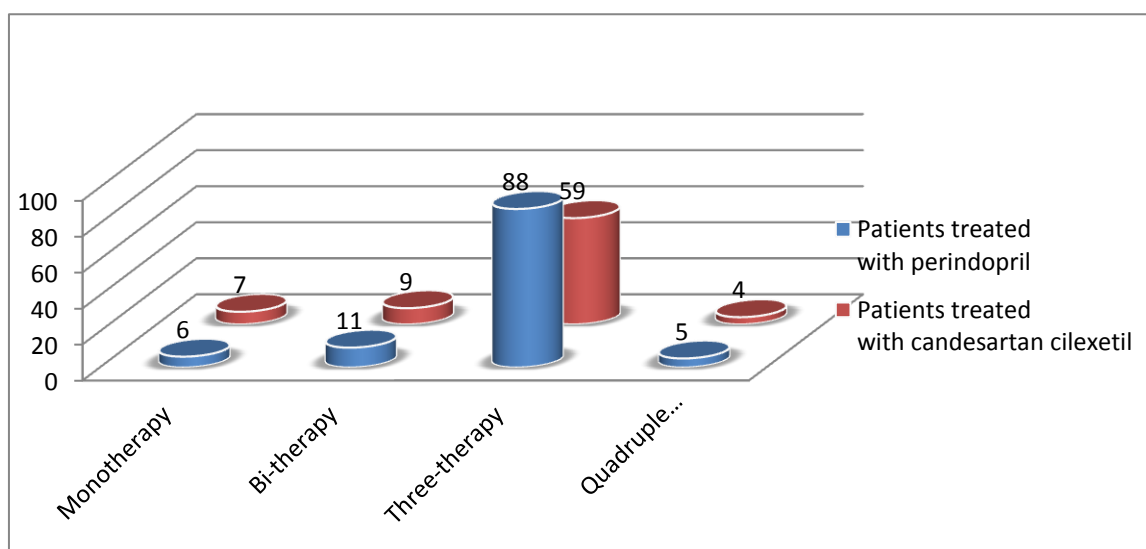


Figure 1. Types of therapies for the two groups of patients

Antihypertensive regimens included: a conversion enzyme inhibitor: perindopril, a receptor AT1 of angiotensin II antagonist: candesartan cilexetil as the main drugs, and besides these, a thiazide-like diuretic was added: indapamide, a beta-blocker: bisoprololulm and, if

necessary, a calcium channel blocker was added also for both study groups: amlodipine. For dyslipidemia the patients were treated with a statin.

The other associated comorbidities (diabetes mellitus, arrhythmias, peripheral circulatory disorders) had a specific medication



(oral antidiabetics, insulines, antiarrhythmics, vasodilators).

Blood pressure and echocardiographic parameters were evaluated initially and after six months

from the beginning. After six months of treatment, systolic and diastolic blood pressure values have been lowered as follows:

Table 3. The evolution of systolic blood pressure values in study patients

No	Type of therapy	Baseline	6 Months	p
1.	With perindopril	150.6±14.6	134.5±24.4	0.0001
2.	With candesartan cilexetil	148.1±25.1	131.7±16.2	0.0006

Table 4. The evolution of diastolic blood pressure values in study patients

No	Type of therapy	Baseline	6 Months	p
1.	With perindopril	88.2±9.8	77.9±6.6	0.0001
2.	With candesartan cilexetil	87.9±12.6	76.2±9.2	0.0001

Systolic and diastolic blood pressure values significantly decreased after treatment for both groups of patients ( $p<0.05$ ). Although the statistical analysis showed a similar reduction in both treatment groups (for systolic blood pressure,  $p=0.36$  and for diastolic blood pressure,  $p=0.14$ ), differences between therapeutical

groups were not statistically significant.

At six months the echocardiographic evaluation showed a reduction of left ventricular mass index, interventricular septal and posterior wall thickness. An improvement on E/A wave ratio has been noticed too. The values obtained are shown in table 4.

Tabel 4. Echocardiographic evaluation

Parameter (mean±SD)	Perindopril group (n=110)			Candesartan cilexetil group (n=79)		
	Baseline	6 months	p	Baseline	6 months	p
Left ventricular mass (g)	229±55.2	209.8±50.4	0.0001	225.5±81.0	203.3±73.1	0.0001
Left ventricular mass index (g/m <sup>2</sup> )	132.5±31.9	121.2±29.1	0.0001	130.4±46.8	117.5±42.2	0.0001
PWTd* (mm)	11.0±1.5	9.9±1.3	0.0001	10.8±1.5	9.8±1.4	0.0001
IVSTd* (mm)	11.2±1.4	10.2±1.3	0.0001	11.4±2.1	10.1±1.8	0.0001
E/A	0.95±0.23	1.05±0.25	0.04	0.88±0.16	0.97±0.18	0.03

\*PWTd: posterior wall thickness in diastole ; IVSTd: interventricular septal thickness in diastole

In the perindopril group, the ventricular mass decreased by 8.38%, ventricular posterior wall thickness and interventricular septum values decreased by 10.00% and 8.92%, and the E/A ratio has been improved by 10.52%.

In the candesartan cilexetil group, the ventricular mass decreased by 9.85%, ventricular posterior wall thickness and interventricular septum values decreased by 9.25% and 11.40%, and the E/A ratio improved by 10.22%.

A percent of 41.77% (n=33) patients treated with candesartan

cilexetil reached the normal values for the left ventricular mass index, while 39.09% (n=43) patients treated with perindopril presented normal values of it.

Among 79 patients treated with candesartan cilexetil, 37 (46.38%) presented concentric left ventricular hypertrophy and 50 of them (63.29%) were diagnosed with left diastolic dysfunction.

The ventricular hypertrophy (assessed as left ventricular posterior wall thickness) did not correlate with diastolic dysfunction (evaluated by E/A), neither in perindopril-treated group ( $r=0.213$ ,  $p=0.285$ ), nor in the candesartan cilexetil group ( $r=0.173$ ,  $p=0.343$ ). Furthermore, the blood pressure values did not correlate with the decrease of ventricular mass index (for perindopril group  $r=0.053$ ,  $p=0.628$ , respectively for candesartan group  $r=0.039$ ,  $p=0.752$ ) or the enhancement of E/A ratio (for perindopril group  $r=0.053$ ,  $p=0.628$ , respectively for candesartan group  $r=0.081$ ,  $p=0.637$ ).

In the study group treated with candesartan cilexetil the percentage of patients who have associated left ventricular hypertrophy and diabetes mellitus was 41.17% compared with those who had left ventricular hypertrophy but did not have diabetes: 23.80%. Similarly, for the group of patients treated with perindopril, 30% of diabetic patients presented left ventricular hypertrophy and only 13% of patients with left ventricular hypertrophy were not diabetics.

#### D. Evaluation of costs

The conversion enzyme inhibitor used was perindoprilum (DCI) with the brand name PRESTARIUM tablets

of 10 mg, an original product. It is administered once a day in the morning.

The receptor antagonist used was candesartan cilexetil (DCI) with the brand name ATACAND tablets of 16 mg, an original product indeed. It is administered once a day in the morning.

The beta-blocker from the therapeutic scheme is bisoprololum (DCI), under the brand name CONCOR COR tablets of 5mg, administered once a day.

The diuretic drug was indapamidum (DCI), with the brand name TERTENSIF tablets 1.5mg and the calcium blocker was amlodipinum (DCI) with the brand name NORVASC tablets 5mg.

The medicines prices for a month of treatment was listed according to Canamed (The National Catalog of Prices of Medicinal Products Authorized for Marketing) 2013.

The patients in the study were evaluated in a day care hospitalization regimen. The direct costs evaluated included: the medical consultation with a cardiologist, electrocardiograms, Doppler echocardiography PW+CW examination, three consecutive blood pressure readings, heart frequency, thoracic radiography, abdominal ultrasound, Holter and the biochemical analysis of blood samples (ESR, blood count, serum creatinine, urea, AST, ALT, potassium, sodium, chloride serum, blood sugar, serum cholesterol, triglycerides, HDL-C, LDL-C, uric acid).

The cost of medical procedures and analysis for a day hospitalization was 233.53 lei the equivalent of 54.17 Euro.

Table 5. The medicines prices according to Canamed 2013

Type of therapy	The therapy with Prestarium cp.10mg (lei/euro)	The therapy with Atacand cp.16mg (lei/euro)
<b>Monotherapy</b>	63.61 lei (14.75 Euro)	71.50 lei (16.58Euro)
<b>Bi-therapy</b> : it was added Tertensif cp.1,5mg	63.61+21.05=84.66 lei (19.63 Euro)	71.50+21.05=92.55 lei (21.46 Euro)

<b>Three-therapy:</b> it was added also Concor cp.5mg ;	63.61+21.05+22.31=106.97 lei (24.81 Euro)	71.50+21.05+22.31=114.86 (26.64Euro)
<b>Quadruple therapy:</b> it was added: Norvasc cp.5mg	63.61+21.05+22.31+19.94=126.91 lei (29.43 Euro)	71.50+21.05+22.31+19.94=134.8 lei (31.27 Euro)

#### E. The incidence of adverse events

There is no case of medicine interruption because of adverse events. The adverse events incidence in the two groups is shown in figure 2.

A frequent incidence of a dry, irritative cough (5.45% versus 2.53%) and of angioedema (0.9% versus 0%) in the patients treated with perindopril comparing with the patients treated with candesartan cilexetil was noticed.

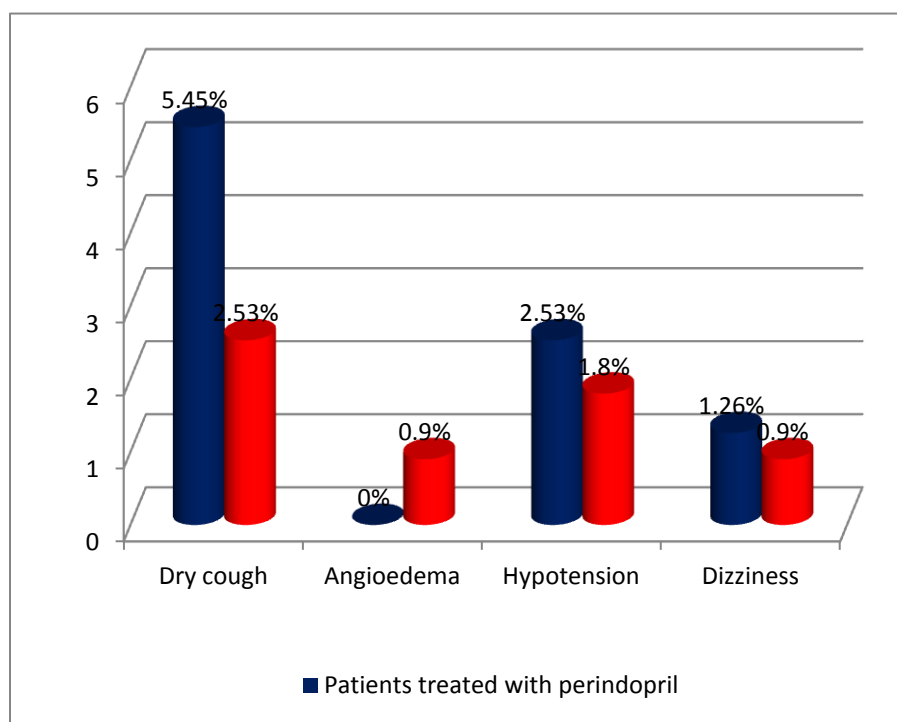


Figure 2. The adverse events of the study patients

## DISCUSSIONS

The study shows that both therapies significantly decrease blood pressure values, a large percentage of patients reaching to the normal values. The statistical analysis did not determine differences between the two types of therapy in this regard.

The two type of active substances (perindopril and candesartan cilexetil) which act on renin-angiotensin-aldosterone system administered to hypertensive patients with high and very high cardiovascular

risk significantly lower parameters that characterize ventricular hypertrophy and diastolic dysfunction (left ventricular mass, posterior wall thickness, interventricular septal wall thickness and E/A wave ratio). The differences between the two classes of medicines are not significant and are in accordance with ONTARGET study [16]. These additional pharmacological effects of inhibitors of renin-angiotensin-aldosterone system determine through complications

prevention (systolic heart failure, coronary disease, stroke), reduction of hospitalization, cardio-vascular morbidities and mortality [11, 14, 21] and by this, will lower the total costs.

The study showed that changes on left ventricular mass volume and other parameters are independent of blood pressure reduction for both substances, which is in accordance with the literature data [10, 12]. So, these agents could represent first line medication, which must be commenced as soon as the diagnosis of hypertension is confirmed.

Although antihypertensive monotherapy is preferable in the early stages of the disease, due to the high incidence of diastolic dysfunction (a precursor for systolic heart failure), with or without left ventricular hypertrophy, antihypertensive therapy should be started with a combination of active substances [1].

The PICXEL and REASON studies demonstrated the therapeutic efficacy of perindopril on hypertensive patients with left ventricular hypertrophy and encouraged the initiation of an antihypertensive therapy with perindopril in combination with a diuretic, such as indapamide. [1, 4, 5]

Furthermore, CATCH, CASE-J, GIFU studies showed that candesartan cilexetil significantly reduces the left ventricular mass index, QT interval electrocardiographic assessed [15], and improve diastolic and endothelial dysfunction after only three months of treatment. [2, 9]

It has been noticed that, on both groups there were patients who had diastolic dysfunction in absence of ventricular hypertrophy. Clinical studies show that diastolic dysfunction is an early sign of heart damage in hypertensive patients and the risk of fatal or non-fatal cardiovascular events significantly and positive correlate with left ventricular diastolic damage in the absence of ventricular hypertrophy [6, 17, 19].

In hypertensive diabetic patients, the treatment with an inhibitor of renin-angiotensin-aldosterone system, determines an important reduction of blood pressure values and echocardiographic parameters, findings that are not confirmed in other studies with calcium channel blockers or with beta-blockers. It could be due to an increased activity of angiotensin II and an up-regulation of myocardial receptors AT1 that have been reported in cases of hyperglycemia. These aspects may lead to myocardial fibrosis associated with increased risk of arrhythmias and myocyte hypertrophy [10]. The high incidence of ventricular hypertrophy in patients with diabetes on both study groups indicates the need for a much closer therapeutic monitoring of this category of patients.

After six months of treatment, there were no cases of medication interruption due to side effects. The incidence of unwanted effects though, was higher in the group treated with perindopril. [4, 5]

## CONCLUSIONS

Echocardiographic evaluation is a very sensitive method, compared to electrocardiogram, for detection of left ventricular hypertrophy and diastolic dysfunction, which should be used as a routine evaluation method in all hypertensive patients regardless of costs. [21, 22]

If left ventricular hypertrophy or diastolic dysfunction is ascertain, treatment with a renin-angiotensin-aldosterone system inhibitor should be initiated.

Comparing the prices of the two therapeutic regimens, corroborating the results in terms of efficacy and in the absence of adverse events, the

converting enzyme inhibitor – perindopril could be considered the first choice medication in our study. These data is supported by the number of patients randomized in the study

groups: 110 patients were treated with perindopril and only 79 patients were chosen to be treated with candesartan cilexetil.

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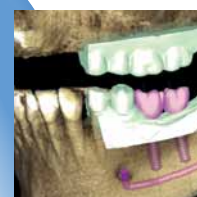
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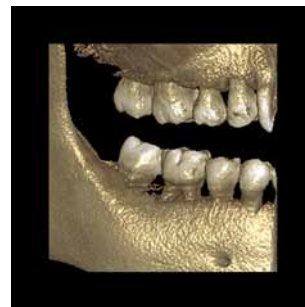
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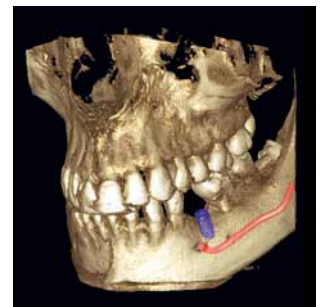
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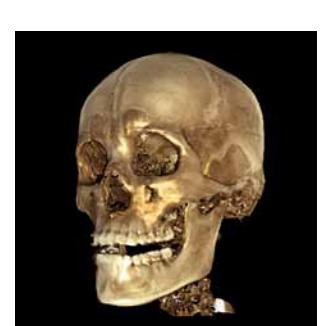
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## **2. FIRST PUBLICATION**

The editorial board will not consider a paper already reported in a published general review or described in a paper proposed to or accepted by another journal. This does not exclude papers which have been rejected by other journals. Also, papers which have been presented at a scientific meeting will be accepted for discussion if they have not been entirely or partially published in a similar publication. „Multiple” publishing of the same study is seldom justified. One of the possible justifications is publishing in a second language but only if the following conditions are met:

- Editors of both journals involved are fully informed;
- Priority of the initial publication will be respected by a minimum publishing interval of two weeks;
- For the second publication, a shortened version will suffice;
- The second version strictly reflects data and interpretations in the first;
- A footnote may state: „This article is based upon a study initially published in [title of the journal]”.

## **3. PATERNITY**

Paternity must reflect the common decision of the coauthors. Each author must have participated enough to take public responsibility for the content. A paper with collective paternity must have a key person responsible for the article.

## **4. COPYRIGHT**

In order to reproduce materials from other sources, written agreement from the copyright owner must be obtained:

- photographer – for unpublished photographs;
- hospital where the photographer (physician) is employed – for unpublished photographs performed during the employment period;
- initial publisher – for a table, picture or text which have previously been published elsewhere.

## **5. ETHICAL ASPECTS**

Do not use name of patients, initials or hospital observation charts numbers. If a photograph of a body part which could allow direct or deductive recognition of the patient needs publishing, then the paper must be accompanied by the written consent of the patient and clinician, as well.

## 6. PRESENTING THE MANUSCRIPT

For the journal „*Medicine in evolution*“, the manuscript must be typed double spaced, on white A<sub>4</sub> paper – 210 x 297mm, on one side (2.5cm upper and lower borders, 3cm left and 2cm right border, respectively), in clear characters, no further corrections or addings. It is advisable that articles are presented on CD or other data transfer methods, in Word format, 12 Times New Roman fonts - using Romanian characters – respecting the same page order, accompanied by a printed version. Graphs – black and white or coloured – may be generated in MS Excel or MS Graph, inserted in the body of the paper or presented in a different file. Infected materials will not be used.

### 6.1. FIRST PAGE (TITLE PAGE)

*Together with the title and names of the authors, the first page must include the affiliation, professional and university degree (if applicable), marked by asterisc for every author; it is advisable to give at least a phone and/or fax number or e-mail address of the first author who may be contacted by the editors for additional recommendations or explanations.*

### 6.2. ABSTARCT OF THE PAPER

#### 6.2.1 Recommendations for original studies

Original studies must include a structured abstarct of maximum 150 words, containing the following titles and informations:

- Aim and objectives;
- Material and methods;
- Results;
- Conclusions;
- Key words: give 3-5 key words;
- The abstract will be translated into an international circulation language.

### 6.3 CONTENT OF THE PAPER

#### 6.3.1 For original articles

The text will usually be divided into sections:

- Introduction – presentation of general aspects, in the context of the approached theme
- Aim and objectives – Define the aim of the article. Briefly expose the rationale of the presented study or observation. Make strictly pertinent referrals and do not exhaustively review the subject. Do not include data or conclusions from the paper.
- Material and methods – Describe the selection of observations or subjects for the experiment (including controls). Identify methods, equipments (with the name and address of the manufacturer in brackets) and give sufficient details on procedures. Give references for the selected methods, including statistical methods; offer details and brief descriptions for previously published methods which are not well known; describe new or

substantially modified methods, justify their use and assess their limitations. Precisely identify all used drugs and chemicals, including generic names, dosage and administration ways. Describe statistical methods with sufficient details for reported results to be verified. Whenever possible, quantify discovered aspects and present them with appropriate measurement indicators for the uncertainty or error of measurement (such as confidence intervals).

- Results – Present results in a logical succession as text, tables and illustrations. Emphasize or briefly describe only important observations.
- Discussions – Underline new, important aspects of the study. Do not repeat in detail data which have been presented in previous sections. Include implications of revealed aspects and their limitations, including implications for future studies. Connect your observations to other relevant studies. Relate the results to the aim proposed for the study.
- Conclusions – organize conclusions which emerge from the study. In the end state: a) contributions to be acknowledged but which do not justify paternity right; b) thanks for technical support; c) thanks for financial or material support.

#### 6.3.2 Indications for case reports

Themes may be selected from all medical fields. Manuscripts which offer a special gain for daily activity will have priority. The title must be clearly, precisely stated. It may be completed by a subtitle. It is advisable to include in the key words of the title the main message, the special element which may be observed from the case evolution. The content of a case report must be divided into three parts:

- Introduction – It must include a maximum of 15 typed rows (half page). Here, the main medical problem is summarized in order to place the case in a specific domain.
- Case report – It contains essential specific information on the case.
- In order to make a logical, chronological and didactical case report the following 5 chapters are needed:
  - I. Anamnesis;
  - II. Clinical examination data;
  - III. Laboratory data;
  - IV. Additional paraclinical investigations;
  - V. Treatment and evolution.
- Discussions – The reason for the case report must be stated. The report must be patient-centered. Occasional deviations from typical (characteristic) evolutions, nosologically important facts must be presented in such a manner to expose the clinical picture as completely as possible. The case report must not appear as an appendix of a general review. Dimensions of a case report: maximum 6-8 typed pages, 30 rows of 60 characters/page.

#### 6.4. MEASUREMENT UNITS, SYMBOLS, ABBREVIATIONS

All measurements must be expressed in International System (IS) units. Abbreviations must be fully explained when first used.

## **6.5. TABLES**

Tables are noted with Roman figures and they will have a brief and concise title, concordant with their content.

## **6.6. ILLUSTRATIONS**

Number all illustrations in Arabic figures in a single succession. Apply a label on the back side of every illustration, containing its number and an arrow indicating the upper side. Coloured illustrations may be accepted but it is the choice of the editors, according to particular technical abilities of each journal issue, or it may involve a fee in special cases.

## **6.7. EXPLANATIONS FOR DRAWINGS AND GRAPHS**

Explanation for drawings and graphs must be clear and in readable dimensions, considering the necessary publishing shrinkage.

## **6.8. PHOTOGRAPHS**

Offer glossy, good quality photographs. Any annotation, inscription, etc. must contrast with the ground. Microphotographs must include a scale marker.

## **6.9. ILLUSTRATION LEGENDS**

Include explanations for each used symbol, etc. Identify the printing method for microphotographs.

## **6.10. REFERENCES**

A numbered list of references must be provided at the end of the paper. The list should be arranged in the order of citation in the text of the publication, assignment or essay, not in alphabetical order (according to the Vancouver rules). List only one reference per reference number. It is very important that you use the correct punctuation and that the order of details in the references is also correct.

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## 7. COPIES FOR PUBLISHING

In order to accelerate publishing, the main author will send a set of printed sheets presenting the final version of the paper, as it will appear in the journal. It is really helpful that texts to be also sent on electronic support, diacritic characters mandatory.

## 8. REJECTION OF PAPERS

If a paper does not meet publishing conditions, whatever these may be, the editors will notify the first author on this fact, without the obligation of returning the material. Original photographs or the whole material will be returned only if the author comes to the editor and takes them.

Papers submitted for publishing will be addressed to:

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