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OUTCOME EXPRESSION IN IDIOPATHIC INFLAMMATORY MYOPATHIES

321.04 - Rheumatology

Summary of Doctoral Thesis in Medical Sciences

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The thesis was elaborated in the Department of Internal Medicine, Discipline of internal medicine-semiology, Discipline of cardiology,
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THE CONCEPTUAL RESEARCH ITEMS

Topicality. The holistic and complex approach of patients with idiopathic inflammatory myopathies (IIM) involves examining, from the perspective of disease activity, the organic damage and the quality of life, components that influence each other. Although IIMs are regarded as treatable conditions, their prognosis is not well known, therefore the disease outcomes available in the literature and prognostic factors vary greatly due to methodological imperfections [1,13].

Description of the existing situation in the research field.

The results of the populational surveys have indicated a bimodal distribution with predilection to age segments ranging from 10 to 15 years in children and 45-60 years in adults [5,7]. The epidemiological data for the adult population recently published in the Euromyositis International Register, presents the IIM prevalence with a variation from 0.55 to 17.50 per 100,000 people, the authors concluding that the rarity and heterogeneity of the disease made it difficult to study this group of diseases through the clinical researches that could provide evidence-based information [6,12,17]. Several sets of diagnostic and classification criteria have been proposed over time, some of which are more useful in medical practice, others ones have been used in clinical trials, making it difficult to compare the results [3,4,8]. Considered to be a group of autoimmune diseases, idiopathic inflammatory myopathies are the result of environmental and genetic factors interaction. Recent hypotheses indicate the presence of a strong genetic association of these groups of diseases with human leukocyte antigen (HLA) class II alleles. Moreover, in the case of idiopathic inflammatory myopathies, infections, exposure to UV rays, vitamin D deficiency, and certain drugs [2,11,18] are considered to be the incriminated environmental factors, although, considered as being treatable diseases, their outcomes, prognosis and prognostic factors vary greatly due to methodological imperfections [14-16]. Also, in the literature, we find that the tendency of knowledgeable researchers in the field was to identify a relationship between the duration of the disease and its consequences, presenting in their publications data on the outcomes of the disease as it ranged from 2 to 9 years without a strict temporal delimitation [9,10 14]. The above mentioned facts have served as a basis for the initiation of a complex research on irreversible changes in idiopathic inflammatory myopathies.

The purpose of the present research was to study the outcomes of idiopathic inflammatory myopathies in order to optimizethe preventive measures.

Research objectives:

1. Assessment of patients with idiopathic inflammatory myopathies according to the ACR / EULAR, 2017 classification criteria.
2. Estimation of the disease outcomes in regards of idiopathic inflammatory myopathies by the myositis damage index.
3. Determining the quality of life of the patients with idiopathic inflammatory myopathy through the SF-8 questionnaire.
4. Assessment of the work productivity and satisfaction regarding medical services of employed patients with idiopathic inflammatory myopathies.
5. Determination of comorbidities in patients with idiopathic inflammatory myopathies.

Novelty and scientific originality of the research study. In thiscrosssectional study there were investigated the clinical and paraclinical outcomes of patients with idiopathic inflammatory myopathies. The criteria for the classification of idiopathic inflammatory myopathies ACR / EULAR (2017) have been applied along this study for the first time. The impact of the disease was assessed considering the quality of life and patient satisfaction.

The scientific problem solved in the thesis is the evaluation of the expression of the consequences of idiopathic inflammatory myopathies and their impact on the patients' life, which contributed to the elaboration of the holistic and personalized algorithm of these patients for further application in clinical practice.

Theoretical significance of the thesis. By highlighting the consequences of idiopathic inflammatory myopathies, the study issued the prototype of the complex evaluation system of patients with MI, identifying the consequences spectrum, the tools for assessing the disease and determining the quality of life, capitalizing on the holistic approach of the patients, which is a factor of major importance in modern medical practice.

Applicative value of the thesis. The study argued that the used clinical tools are necessary and informative in assessing the consequences in patients with idiopathic inflammatory myopia. The results of the research contribute to the study of the consequences of idiopathic inflammatory myopathies and to the elaboration of PCN-319 (approved by the MSMPS Order of the RM No. 382 of 07.03.2018).

The main scientific results forwarded to the thesis approval:

- identification of clinical and paraclinical outcomes, and assessment of the methodology of evaluation of the patient with MI;
- using the achieved information on the application of the myositis damage index and its subsequent management;
- assessing the impact of disease consequences on the patient quality of life;
- development of an algorithm for evaluation and medical management of patients with MI.

Implementation of scientific results. The results of the study were considered to have scientific value and were included in the provisions of the National Clinical Protocol 319, "Idiopathic inflammatory idiopathic myopathies", as well as in the didactic activity of the Department of Internal Medicine.

Approval of scientific results. The results of the research were reported in 15 national and international forums; international congresses: The 6th International Medical Congress for Students and Young Doctors „MedEspera", Chișinău, 2016; Annual European Congress of Rheumatology – EULAR, Madrid, 2016; Annual European Congress of Rheumatology – EULAR, Amsterdam, 2018; the XXIIIth National Congress on Rheumatology, București, 2016; The 35th Balkan Medical Week, București, 2016; The 36th Balkan Medical Week, Sofia, 2017; Annual European Congress of Rheumatology – EULAR, Londra, 2017; The International Medical Student's Congress of Bucharest 6th -10th of December, 2017; The 7th International Medical Congress for Students and Young Doctors „MedEspera", Chișinău, 2018; The 37th Balkan Medical Week, Atena, 2018; the XXVth National Congress on Rheumatology, București, 2018; 3rd Global Conference on Myositis, Berlin, 2019, national congresses: national congress "Sport.Olimpism. Sănătate", Chișinău, 2017, University Days and the Annual Scientific Conference of the Collaborators and Students SUMPh „Nicolae Testemiţanu", Chişinău, 2017, 2018;

The thesis was discussed, approved and recommended for defense at the meeting of the Discipline of internal medicine - semiology, Department of Internal Medicine of the State University of Medicine and Pharmacy "Nicolae Testemitanu" of the Republic of Moldova (protocol No 4 of 21.12.2018) and Scientific Profile Seminar on Rheumatology 321.04 (protocol No 1 of 14.05.2019)

Publications on the thesis. Study materials were reflected in 32 scientific publications, including 8 articles in reviewed journals, an author's publication; presentations and abstracts in 3 national and 14 international scientific conferences.

Key words: idiopathic inflammatory myopathies, outcomes, modern clinical tools, quality of life.

The study received the approval of the Research Ethics Committee (No. 66 of 23.05.2016) of the USMF "Nicolae Testemitanu".

Summary of the thesis compartments. The paper is exposed on 106 pages of electronic text and is divided into: introduction, 5 chapters, conclusions and practical recommendations. The bibliographic index quotes 236 literary sources. The thesis is illustrated with 20 tables, 31 figures and 10 annexes.

THE THESIS CONTENT

INTRODUCTION

The Introduction section addresses the theoretical aspects of the components analyzed in the research, the importance of the approached topic, the aim and objectives of the study, the scientific novelty of the obtained results, the theoretical importance and the applicative value of the work, the results approval, and the summary of the thesis compartments.

1. APPROACH TO PRECIOUS AND TARDIN CONSEQUENCES OF IODIOPATIC INFLAMMATORY MIOAPPIES

(Literature review)

Chapter 1 represents the synthesis of data present in the literature with reference to current epidemiological data, the pathogenetic mechanisms incriminated in the myopathic process, but also the outcomes of idiopathic inflammatory myopathies reported in various publications of the known researchers.

2. GENERAL AND SPECIAL ASSESSMENT METHODS OF THE PATIENTS IN THE STUDY GROUP

2.1 Clinical-statutory characteristics of the study group

According to the purpose and objectives of the thesis, we planned a transversal study, so we selected a group of patients with MII diagnosis that was examined according to the design of the study (figure 1), by general and special methods. The general exam included interrogation, clinical research on systems and organs, anthropometry, markers of inflammation, serum glucose, lipids panel, urea and creatinine.

Inclusion Criteria in the study:

Age over 18 years

Diagnosis of IIM determined according to ACR / EULAR, 2017 criteria

Disease duration longer than 6 months

Patient informed consent

Exclusion criteria from the study:

Patient's refusal

Pre-existing neuromuscular diseases

IIM associated with neoplasia or postinfectious

Myopathy induced by drugs or toxins (statins, GCS, alcohol)

Associated other rheumatic diseases

The characteristics of the socio-demographic parameters of the patients in the study group showed the predominance of women, with female / male ratio 3,2:1, according to the distribution of the residence environment we found a distribution of 55,2 % in the rural environment and 44,8

% of urban cases. Patients included in the research had medical insurance. To be noted that 28 (41,8 %) patients had different degrees of disability, assessed according to the National Council for the Determination of Disability and Labor Capacity [19]. Regarding the marital status of studied group of patients, we found the prevalence of married subjects in 61 (91,00%), widowed, divorced and single each by 2 (2,98 %) cases, respectively. Note that 33 (49,25%) patients out of 67 live with their spouse or partner, others 3 (4,47 %) share home with children, other 2 patients said they lived alone at the time of research.

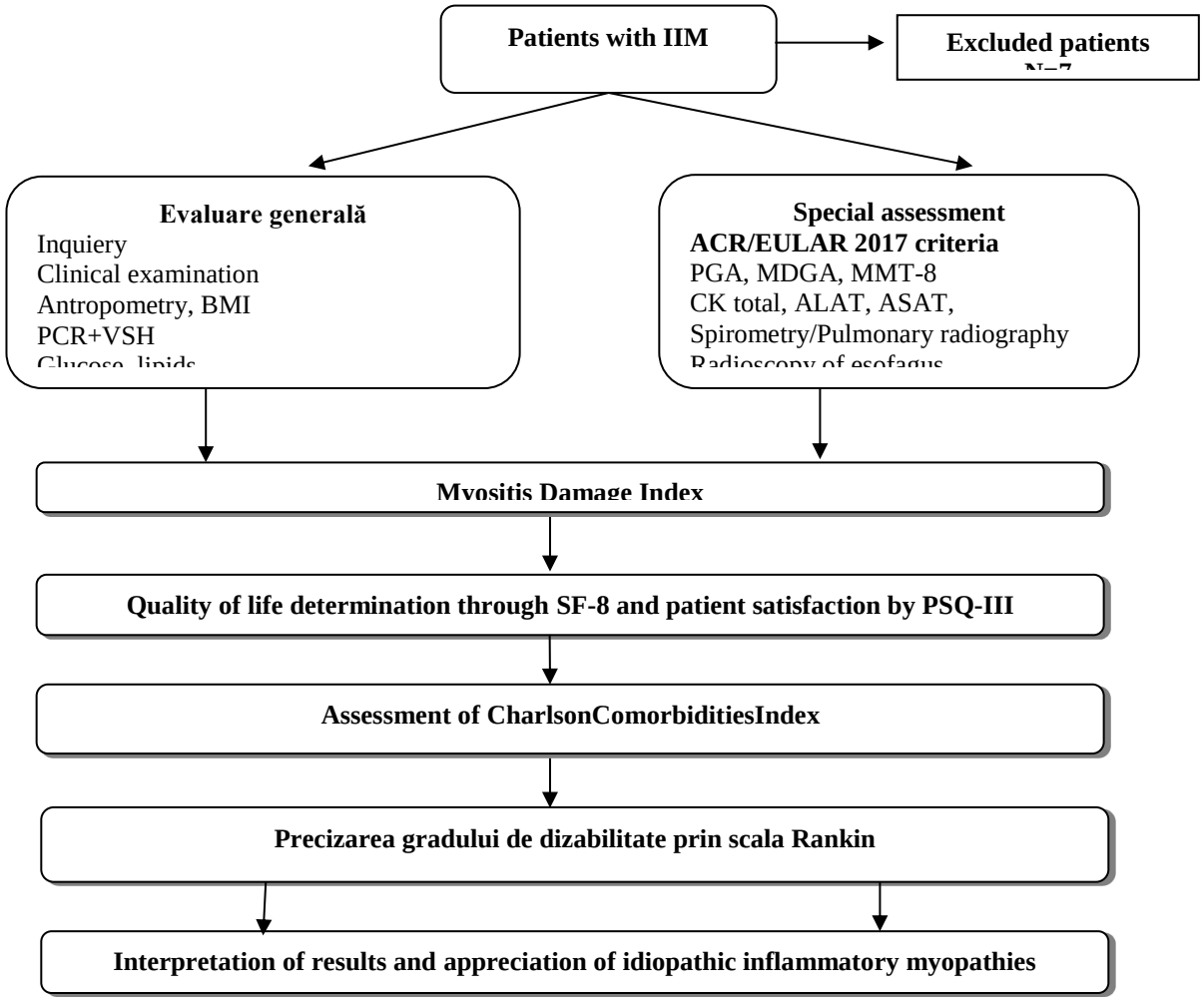


Figure 1. **Study design**

According to IMACS recommendations, patients with myopathies should be assessed through the disease activity, outcomes, so specific efficacy clinical tools have been developed and validated. In order to assess the disease activity, were used the Medical Doctor Global Assessment of Activity (MDGA), and the Patient Global Assessment of Activity (PGA) utilizing the analogue visual scale (VAS) and manual 8 muscle groups-Manual Muscle Test 8 (MMT-8). In order to quantify the irreversible lesions of the disease, the Myositis Damage Index measures the degree of disease on all organ systems, consisting of a series of organ questions, specific to the presence or absence of a certain sign or symptom. Its composition includes the muscular, skeletal, cutaneous, gastrointestinal, pulmonary, cardiovascular, peripheral vascular, endocrine, ocular lesions, and malignant tumors and infections. Another aspect of interest was the presence of co-morbidity in patients with myopathies, assessed through the Charlson Comorbidity Index, and adjusted for age, through which we determined the concomitant pathologies. This questionnaire includes 15 pathological entities and predicts the estimated survival rate at ten years for the patient. We continued the quality of life survey in the Short Form-8 (SF-8) questionnaire, which is a generic

tool for measuring the quality of life of patients with various diseases. It consists of 8 questions, which encompass eight domains: physical function, social function, role limitation (physical and emotional), mental health, vigor, somatic pain, and general health. The interpretation of the results is done through the mental components and physically, the values obtained in patients were reported to the reference population-healthy population. The Patient Satisfaction Questionnaire III version III (PSQ-III), was used to determine the satisfaction of patients with MI and the quality of medical services. The PSQ-III questionnaire consists of 50 items grouped in 7 subscales: general satisfaction, technical quality, interpersonal issues, communication, financial aspects, time spent with the doctor, access / availability / comfort. Work Productivity and Activity Impairment Questionnaire: General Health (WPAI: GH) V2.0 is a validated tool for determining work capacity, consisting of 6 questions addressed to the patient, related to the last 7 days. The obtained results are expressed in percentages with a variation from 0 – no loss of working capacity, up to 100% - total loss of work capacity. The modified RANKIN scale was used to assess disability in patients with myopathies and is a gradual instrument depending on the patient's ability of self-care with range from 0 - lack of disability to 5 - total dependent and 6 - death.

2.3. Methods of Statistical Data Analysis

The data collected from the examined patients was entered into an Excel database and processed in the statistical software MedCalc version 12.7.0, using variational, correlative and discriminatory analysis methods. The Pearson correlation coefficient was applied to determine the degree of correlation between the studied parameters. The correlation coefficient is interpreted in parallel with the p value, which is the probability of obtaining the present results, if this probability is less than 5% ($p<0.05$), then the correlation coefficient is statistically significant. The conclusive differences between the mean values of the studied parameters in different lots was determined using the t-Student criteria. The Box-Plot analysis allowed the graphical representation of the distribution of maximum - minimum values, arithmetic mean and standard deviation for each variable.

3. CLINICAL AND PARACLINICAL APPROACH OF IDIOPATHIC INFLAMATORY MYOPATHIES OUTCOMES

3.1. Characteristic of clinical-demographic parameters of patients with myopathies

Thus, the study group consisted of 67 patients with the genuine diagnosis of idiopathic inflammatory myopathy. One important social aspect in the IIM is the level of training of the persons included in the research, so we were tempted to examine the research group by hierarchizing the years of study less than 9 years, 9-12 years and more than 12 years of education. In addition, patients with education below 9 years old consisted of 5 (7,46%) in the study group, when the share of subjects with 9-12 years of study, which means secondary, high school or college education, was 29 (43,28%) cases. The level of university education, which involves more than 12 years of study, was established in 49,25%, including 7,5% with master studies. In conclusion, we could say that 2/5 had university studies, supplemented with postgraduate studies by master. At the same time, we were interested in analyzing employment, with data showing that at the time of research one-third of the patients were employed, including 10 (14,92%) full-time and 9 (13,43%) with part-time. Note that 7 (10,45%) patients were unemployed, did not have a job and did not carry out an activity to earn income. In fact, 2 (2,99%) were households – persons that have only household activities and are not looking for a job. Patients retired due to age limit were 13 (19,41%) at the time of the study. We have used the Kuppuswamy socio-economic status, revised in 2014. We found that 7 (10,45%) patients were trained, including doctors, school

teachers, accountants, 14 - semi-professions (eg nurse), 18 others (26,86%) were farmers, clerks or service providers. Workers were divided into three groups, qualified - 20 (29,85%), and unqualified - 8 (11,94 %) cases. Therefore, the professional profile was expressed by semi - profession, farmers and service providers. We were interested in analyzing the group of patients with IIM according to the age characteristics, so it was found that at the time of the research, the mean age was 53,1 ± 12,5 years, while patients aged 25-78 years were examined. Note that at the time of research, only 7 (10,45%) patients were younger than 35 years old, considered young adults, 15 (22,38%) cases between 36-50 years old, other subjects had over 50 years old. We were interested in studying the age distribution of patients at the onset of the disease, so we determined that in 18 (26,87%) subjects the diagnosis of IIM was established till 35 years, followed by 22 (32,84) in which disease started at the age of 36-50 years and respectively the group of patients with the disease onset after 50 years - 40,29% of the cases, working-age subjects. Note that the mean age of the study group was 45,0±13,4 years. We analyzed the duration of the disease, and determined the oscillation with wide varied ranges, from 6 to 324 months, with an average of 98,1±72,9 months, which is about 8 years. Regarding the time frame from the onset of the first symptoms till the diagnosis establishment, we found that in average it was 5,3±9,1 months, varying from 0,5 to 35 months.

3.2. Patient evaluation through the ACR / EULAR Classification Criteria for Idiopathic Inflammatory Myopathies

We continued the research by retrospective analysis of the clinical manifestations at the onset of the disease on study patient, using the set of ACR / EULAR classification criteria for idiopathic inflammatory myopathies validated in 2017. We analyzed the obtained results through these criteria by dividing the parameter age at the disease onset in two categories up to 39 and 40 yearsold,and more than 40 years old, topography of muscle asthenia, cutaneous characteristics manifested by heliotrope rash, papules and the Gottron sign. At the same time, dysphagia was presented as an individual clinical parameter, together with laboratory variables and muscle biopsy findings. From the obtained data is clear that 24 (35,82%) of subjects had the onset of the disease up to 39 years old, and in 43 (64,18%) the symptoms appeared after 40 years old. We continued the investigation by exploring each variant of muscular asthenia separately. Thus, the progressive proximal symmetric weakness of the upper extremities was determined in 66 (98,51%) cases, being the most common clinical variable present at the onset of the disease, followed by the proximal progressive symmetric weakness of the lower extremities in 64 (95,52%) patients. It should be noted that of the 67 patients enrolled in the study, in 56 (83,58%) was determined the proximal lower muscle weakness more evident than in the distal muscles, and in 17 (25,37%) patients the flexor muscles of the neck, were weaker than the extensions group.

The cutaneous expression in the study group was determined by the prevalence of heliotrope rash, characterized by periorbital violaceum erythema, accompanied by eyelid edema - 35 (52,23%), Gottron papules, located on the dorsal side of metacarpophalangeal and interphalangeal joints - 26 (38,81%) cases, and uncommon, the Gottron sign was observed in 6 (8,95%) patients. The presence of dysphagia communicated by the patient as a difficulty in swallowing solid and liquid foods, was detected in a group of 13 (19,41%) patients.

Patients were examined for the at least one laboratory variable, which were determined in different levels, such as serum creatine kinase, lactate dehydrogenase / aspartate aminotransferase or alanine aminotransferase. We were interested about the anti-Jo-1 antibody phenomenon, examining each patient on the grounds that, in the authors' opinion, antiJo-1 remains a specific

antibody and contributes to a higher score in the new criteria for classification of myopathies. Of the 56 subjects examined by this index, an increased level of anti-Jo-1 was found in only 7 (10,45%) cases. Despite the low frequency of anti-Jo-1 antibodies, the patients included in the study met the new classification criteria. According to the new set of criteria, muscle biopsy was declared optional and in the study group was performed in 17 (25,37%) patients with MII. Among the typical findings identified in biopsy, endomisial and perimisial infiltration were established in 9 (13,43%) and 8 (11,94%) cases, respectively. Perifascicular atrophy and framed vacuoles were found in 4 (5,97%) and 5 (7,46%) patients, respectively. Thus, we can summarize by the detected characteristics, that the number of criteria present in the studied patients was 7,52±2,21, with a variation interval from 5 to 11 criteria, which constituted 91,4±14,5 percent cases. This fact enabled the diagnosis of idiopathic inflammatory myopathy and patients inclusion in the study. By conducting the research process, in order to compare the groups, we divided the study group according to the duration of the disease; group I included patients with MI between 6-24 months, considered early MI and group II - over 24 months, considered to be an established or late illness. Thus, patients in group I met 7,58±1,95, and those in group II with 6,66±1,69 new classification criteria ($p>0.05$).

3.3. Assessment of disease activity in patients with idiopathic inflammatory myopathies

From the outline goals point of view, idiopathic inflammatory myopathies could be assessed through the disease activity and its consequences. In this context, we were interested in studying disease activity in the patients in included in the investigated group. To be noted that according to IMACS recommendations, disease activity is quantified by the manual muscle test - MMT-8, PGA and MDGA (VAS). In the following graphic (figure 2) it is presented the box-plot analysis of the determined values of the patients in the investigated group. Thus, we noticed a patient overvaluation of their overall condition by PGA-43.96 (i-v 5-100) mm versus MDGA, indicating 37.45 (i-v 5-100) mm ($p\leq0,05$).

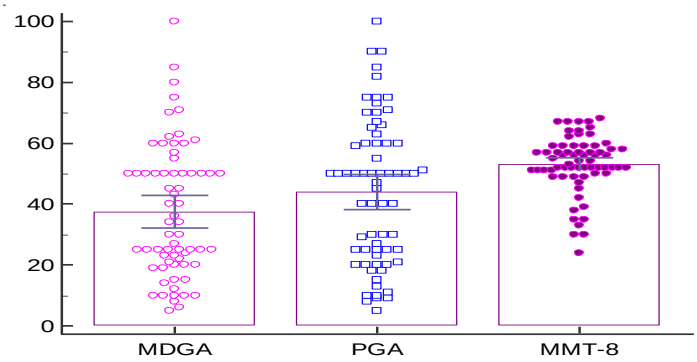


Figure 2. **Disease activity according to PGA, MDGA și MMT-8 (box-plot)**

Determination of muscle strength by MMT-8 revealed – 53,03 ± 9,39 (i-v 24-67) points, interpreted as moderate muscle strength. We directed the research vector to analyze the myopathies activity according to the duration of the disease, to analyze the patient's overall assessment values as compared to the doctor's assessment. We found that the data showed that in the lot the value PGA was 38,50 mm versus 45,67 mm, lot II.

Analysis of the results implies that patients up to 2 years of illness had their generally lower functional status compared to subjects over 2 years of illness. We continued the research by analyzing the indexes at the doctor's assessment over the same time period and we found that MDGA was 34,69 and 38,31 in groups I and II, respectively.

Table 1. **Disease activity depending on the duration of the disease**

Variabile	MMT-8	PGA,mm	MDGA,mm	p
Disease activity <2 years	52,44±12,36	38,5±26,39	34,69±24,5	>0,05
Disease activity>2 years	53,22±8,39	45,67±23,21	38,31±20,93	<0,05

Thus, we believe that in the first 2 years of illness, both in the patient and doctor assessment, the overall status was low, the patient overestimated his condition (p>0,05). Regarding patients in group II, the data of both evaluators were 45,67vs 38,31 mm. The data in Table 1 shows a decrease in the muscular manual test in both groups, more obvious in lot I, making up 50,44, being 63,05% of the maximum possible score, when in lot II – 66,52% of the maximum MMT score.

We were interested in analyzing the evolution of the disease in the study group patients, so from the presented data we found out that 8 (11,94%) subjects had monocyclic type of evolution of the disease, 42 (62,68%) cases polycyclic evolution and 17 (25,37%) - chronic disease progression. In conclusion, patients with MII in the studied group presented with moderate activity of the disease with predominance of polycyclic evolutionary type, identified in about 63% of cases.

3.4. Assessing the outcomes of the disease by myositis damage index

According to the study design, we continued the research by assessing the outcomes of the disease through validated clinical tools to encompass the multisystem damage. In the context of the presented ones, we intended to identify the spectrum of complications of the disease by applying the myositis damage index to the patients in the study group. As first item of interest was the muscular atrophy, clinically reported in 23 (34,33%) patients, especially in the thigh muscles. Note that the decrease in muscle volume confirmed by imaging methods, was established in 10 (66,66%) cases of 38 investigated patients. Thus, in the evaluation of irreversible manifestations we found the muscular dysfunction manifested by the decrease in capacity for aerobic exercises, was present in 36 (53,73%) subjects. Since serum creatinine with values below the admissible norm is an indicator of reduced muscle metabolism, we were interested in determining its serum concentration, so a low titration was found in 18 (26,86%) patients. Another component of the myositis damage index was joint contracture, in the study group was found in 3 (4,47%) patients. We continued the evaluation by determining osteoporosis in the presence of fracture or vertebral collapse, which was detected imagistically in 4 (5,97%) patients. Another indicator of skeletal interest was osteoporosis without clinical fracture, and it was detected in 36 (53,73%) subjects. Avascular necrosis was important through the pains induced by it. For easy-to-understand reasons we used we used for diagnostic imaging methods, avascular necrosis being detected in 5 (7,46%) patients. Joint deformities, including reductible deformities, were identified in 3 (4,47%) patients. We then carefully evaluated the movement limitations, limitations in extension and flexion of the elbow, knee extension and ankle dorsiflexion, and they were found in other 3 (4,47%) subjects. Muscle weakness that can't be attributed to an active muscular disease has not been identified in the study group, as it was an exclusion criteria from the research.

In the following material we analyzed the musculoskeletal lesion in 2 groups of patients with IIM, depending on the duration of the disease. Thus, group 1 study consisted of 16 patients with disease duration up to 2 years, and group 2 - patients, duration of illness was more than 2 years, 51 patients respectively. The data analyzed revealed that muscle atrophy as a result of the disease was determined in both groups of study. It should be noted that 3 (18,75%) cases of atrophy

were present in the group with early IIM- up to 2 years, and in group II, 20 (39,21%) patients had a muscular atrophy detected by the doctor. In the same time imaging confirmation constituted 66,66% vs. 70,8% in groups I and II, respectively, was higher. Analysis of muscle dysfunction depending on the duration of the disease noted that 8 (50,00%) case with disease less than 2 years and 28 (54,90%) - more than 2 years. Reduced serum creatinine was found more frequently in group II of 6,25% and 33,33% of cases, respectively. Thejoint contracture was present in early IIM in only 6,25% of cases, and 3 (5,88%) was found in group II. Data on osteoporosis in the presence of fracture or vertebral collapse revealed the predominance of patients with disease duration of more than 2 years - 4 (7,84%) subjects. Note that osteoporosis without clinical fracture was found in 36 (53,73%) subjects, of which 4 (25,0%) and 32 (62,74%) cases in groups I and II, respectively. Avascular necrosis was detected in 5 (7,46%) patients who had more than 24 months since the disease onset. The joint deformities were identified in 7 (10,45%) patients, mainly after 2 years of illness - 6 (8,95%) vs. 6,25% with disease duration under 2 years. According to the present data, the movements limitation of was mainly found in patients with disease duration of more than 2 years - 11 (16,41%) patients.

Afterwards, we continued with the skin lesion analysis according to myositis damage index, thus revealing that cutaneous interest is calcinosis, which involved 4 subtypes: nodules, tumor, plane and exoscheleton / calcinosis universalis. Thus, we identified calcinosis in 6 (8,95%) patients, 3 (4,47%) cases of subcutaneous nodules localised on the forearm and thigh, another patient showed plane calcinosis in the depth of the thigh muscles, and 2 (2,98%) patients had diffuse calcinosis. At the same time, the tumor type of calcinosis was not identified in the investigated patients. Scalp involvement was present with focal and diffuse alopecia in 28 (41,79%) patients. Note that 25 (37,31%) patients had alopecia in single or multiple outbreaks. In other 3 (4,47 %) patients diffuse alopecia was detected. Other skin lesions such as cut scars were evaluated in 3 (4,47%) patients. Poikiloderma translated as areas of hyper / hypopigmentation, accompanied by thorax localized teleangiectas, was identified in one patient. Thus, lipodystrophy has been identified in 3 (4,47%) dorsal part of the thighs. We were further interested in analyzing the skin lesions detected in the patients in the study group in terms of the division into the two above-mentioned lots, 1- with the duration of the disease less than 2 years and the second group with a disease progression of more than 2 years , respectively. According to the data analyzed, 3 (4,47%) patients were identified as nodular form of calcinosis, they had a disease duration of more than 2 years, similarly we determined for the subject with plane calcinosis and for the 2 (3,92%) cases of diffuse calcinosis. In the group with a disease duration of up to 2 years, we did not detect patients with calcinosis. Alopecia was present in 28 (41,79%) patients in one case I and 27 (52,94%) in group II. Thus, injuries such as skin scars that were evaluated in 3 (5.88%) patients, poikiloderma identified in one patient and lipodystrophy - 3 (5,88%) patients were detected in subjects with disease duration for more than 24 months.

We later analyzed each sign of organic involvement in terms of the gastrointestinal system, one of the frequent impairments in IIM and included in the myositis damage index. To evaluate this system we used clinical, radiological and ultrasound data. The data revealed the presence of dysphagia in patients in the study group, found in 34 (50,74%) cases. Gastrointestinal abnormal motility, expressed by constipation, diarrhea and abdominal pain, was reported by 22 (32,83%) patients with constipation predominance in 13 (19,40%) patients. In the research group, intestinal infarction was detected in a patient who had good outcome resection of the intestine. Hepatic steatosis was imagistic documented in 18 (26,86%) patients.

In order to compare the data obtained from the application of the index to the digestive tract in patients with myopathies, we divided the study group into two groups depending on the duration of the disease, thus the presence of dysphagia was identified in 34 (50,74%) patients in the study group, in 7 (43,75%) subjects was installed during the first 2 years of the disease, and more frequently, 27 (52,94%) occurred after the 2 year disease period. Gastrointestinal abnormal motility was found more robust in the patients with more than 2 years of disease in 19 (37,25%) patients vs 3 (18,75%) cases with disease progression of less than 2 years, respectively. Note that the case of intestinal infarction occurred in the patient with IIM after 9 years of illness. According to the data, hepatic steatosis was documented in 2 (12,5%) patients with disease duration less than 24 months and 16 (31,37%) with a duration greater than 2 years.

We continued the investigation by assessing the respiratory system because it is involved in the primary pathological process of IIM or as a complication of interstitial lung disease, ventilator insufficiency, PHT, aspiration pneumonia, or pulmonary heart development. In this regard we analyzed the pulmonary items included in the myositis damage index. Data on pulmonary involvement revealed dysphonia, the most common injury - in 19 (28,35%) patients. Impairment of pulmonary function due to respiratory muscle damage was detected in 4 (5,97) patients. The diagnosis of pulmonary fibrosis was established in 18 (26,86%) patients based on clinical signs and paraclinical results, and pulmonary hypertension - 6 (8,95%) cases. Decreased pulmonary function in pulmonary functional tests was identified in 7 (10,45%) patients (i.v. FEV 1 61-74% versus 80-100%). For the comparison of the batches regarding lung lesions we analyzed the data in 2 batches depending on the duration of the disease. According to the data, we established that dysphonia was detected in 5 (31,25%) cases in group I and 14 (27,45%) subjects over 2 years, which coincided with increased disease activity. The modified pulmonary function due to respiratory muscle injury was detected in 1 and 3 (5,88%) patients in group I and group II, respectively. It is clear that in group 1 - the duration of illness under 2 years, pulmonary fibrosis was established in 3 (18,75%) patients, and in group 2 there were 15 (29,34 %) patients who had suggestive clinical signs and specific imaging results. Pulmonary hypertension was found in 6 (8,95%) cases, as well in one and 5 (9,80%) patients, respectively group I and II study. Note that the reduction in pulmonary function found in the investigated patients was diagnosed in only one patient with disease progression below 24 months and 6 (11,76%) subjects with a duration greater than 24 months.

Another group of outcomes according to the myositis damage index which worsens the prognosis of idiopathic inflammatory myopathiesis represented by cardiovascular diseases. We continued the research by assessing cardiovascular and peripheral vascular lesions found according to myositis damage index in the patients included in our study. The present data revealed elevation of blood pressure over a period of 6 months and requiring antihypertensive treatment was found in 28 (41,79%) patients. Another variable of interest was ventricular dysfunction, identified echocardiographically in 7 (10,45%) patients. Ischemic heart disease expressed by angina pectoris with episodes present during the last 6 months was found in 3 (4,47%) cases, and electrocardiographically documented myocardial infarction and specific troponin and CK-MB enzymes were diagnosed in a male in the study group, 60 years of age, 12-year disease with 15 mg Prednisolone dose. Peripheral vascular damage manifested by venous or arterial thrombosis accompanied by edema, ulceration or venous stasis was established in 3 (4,47%) subjects. Claudication manifested by leg painful cramps, predominantly in calves, physical exercise and decreasing after 1-2 minutes of rest, caused by atherosclerosis of lower limb arteries, was reported

in 2 (2,98%) cases. Tissue loss was established in 4 (5,97%) patients, of which finger was amputated in one patient. The research continued with the analysis of cardiovascular and vascular - peripheral injuries in the two study groups, thus the hypertension was found in 4 (25,00%) patients - the duration of less than 2 years and 24 (47,05%) of them disease over 2 years. It should be noted that ventricular dysfunction was identified in both groups of patients, 2 (12,5%) and 5 (9,80%) cases, respectively. Both the 3 (5,88%) cases of angina pectoris and the patient with myocardial infarction were found in the group with the duration of the disease for more than 2 years, as well as the injuries of the peripheral vascular system identified in the study group were found only in patients with disease evolution over 2 years.

By conducting the research we were interested in studying the involvement of the endocrine system in patients with idiopathic inflammatory myopathies. From the available data, we have found that 26 (38,80%) patients developed hirsutism. Thus, 8 (15,68%) patients had reported irregular menstruation, and secondary amenorrhea was identified in 13 (25,49%) women. Diabetes mellitus diagnosed with elevated glucose blood glucose or modified oral glucose tolerance test was found in 6 (8,95%) patients, determined by the endocrinologist. We drew attention to a sign such as dyslipidemia, which was detected in 24 (35,82%) patients. Also in the endocrine system it was necessary to appreciate the sexual function expressed through sexual dysfunction - the patient's dissatisfaction with sexual function (feminine or masculine) and infertility, in the investigated group we found 16 (23,88%) cases of sexual dysfunction, infertility was not declared. Growth failure and delayed occurrence of secondary sexual characteristics were not determined in the study group due to the lack of patients under the age of 18 and, were criteria for exclusion from the research. From the evoked results, we detected that diabetes was present in one case in the first 2 years of the disease and 5 (9,80%) - 2 years after the onset of myopathy. Regarding irregular menstruation, 5 (31,25%) patients declared it in the first 2 years of illness and 3 (5,88%) of them appeared after 2 years. It should be noted that secondary amenorrhea was identified in 13 (25,49%) women who had the disease duration longer than 24 months, it should be noted that in 6 (8,95%) cases from the second group, amenorrhea occurred after total hysterectomy caused by the presence of uterine fibroids. Notable that in the investigated patients we determined the predominance of subjects with diabetes who had the disease duration for more than 2 years - 4 (7,84%) cases versus 2 (12,5%) patients in lot 1. Also within the endocrine system it was necessary to appreciate sexual function expressed through sexual dysfunction - patient dissatisfaction with sexual function (feminine or masculine) and infertility, we found 16 (23,88%) cases of sexual dysfunction, infertility was not detected. I have drawn attention to a sign such as dyslipidemia, was found in 24 (35,82%) patients, in 18 (26,86%) of the disease duration was more than 24 months.

By continuing to determine the items based on the myositis damage index, we had focused on eye injury, infections, malignant tumors and death. Data analysis denotes that ocular impairment translated by decreased vision in the presence or absence of cataracts was established in 19 (28,35%) patients. It should be noted that 4 (5,97%) patients were diagnosed with cataract with the need for surgical replacement with artificial crystal. Another 15 (22,39%) patients had gradual vision loss in the absence of cataracts, with various causes such as diabetic and hypertensive retinopathy, presbyopia, etc.

The opportunistic infections associated with the myopathic process were found in 17 patients, among them 9 (13,43%) cases of chronic infections caused by Candida albicans, cytomegalovirus, staphylococcus aureus, E. coli and 5 (7,4%) with Herpes zoster in 3 (4,47%)

patients associated with multiple infections. In the study group, there was present an acase of a patient with malignant tumor - basalioma with preauricular localization, histologically confirmed and surgical excision treatment. A separate interest was the identification of deaths, 2 (2,98%) of patients died during the study, the cause was aspiration pneumonia and interstitial lung disease. We further categorized the patients in the study group according to the duration of the disease. The results highlighted are that in 4 (5,97%) patients cataract started after at least 2 years of illness. The gradual reduction in vision in the absence of cataract, of different etiology, was detected in one subject in the first 2 years of the disease, and 14 (27,45%) patients perceived it after 2 years of onset of the disease.

According to chronic opportunistic infection data, 2 (12,5%) and 12 (23,53%) patients, respectively, were found to be in lot 1 and 2, respectively. Multiple infections were also detected in a patient with disease duration of less than 2 years and in 2 (3,92%) cases with a disease of more than 2 years. The case of malignant tumor, occurred 12 years after the onset of the disease in a patient from lot 2. It should be noted that both cases of death occurred 2 years after the onset of idiopathic inflammatory myopathy.

According to the application of the myositis damage index we determined the variability of the lesions in the patients in the study group, it should be mentioned that in the average of each patient with idiopathic inflammatory myopathy it corresponded to 7,63±4,46, with a variation interval of 1-13 lesions and the duration of the disease has a moderate impact on the number of irreversible injuries identified in patients, $r = 0.33$; $p<0,05$.

4. CLINICAL-EVOLUTION, INTERRELATION AND OUTCOMES OF IDIOPATHIC INFLAMMATORY MYOPATHIES

4.1. Damage in idiopathic inflammatory myopathies

In the study material, we found complications of the disease that occurred 6 months after the onset of myopathy but not included in the myositis damage index. Thus, being guided by the literature data, we identified a series of complications with different rates of occurrence, such as cardiovascular damage identified by rhythm and conduction disorders, Raynaud's syndrome, livedo reticularis, the delay of the remission of the disease, the disability, we applied the questionnaire directed to these indicators [3,5].

According to the data presented in Table 2, where we presented the consequences of the disease not stipulated in MDI, we found that disability is an important outcome of the disease, and the results are confirmed by the Rankin scale, so disability according to grade 0 signifying the absence of symptoms in the investigated group has not been identified. Patients who presented grade I - without significant disability despite symptoms or symptoms did not interfere with their normal daily activity, 21 (31,34%) cases were in the study group. Mild disability or incapacity to perform all previous activities, but can take care of itself without help, grade II was identified in 24 (35,82%) subjects. In 11 (16,41%) patients, moderate or mild disability was established, the symptoms significantly restrict the patient's usual activities and prevent him from having a completely independent life (but he can go without help). In addition, IV, moderate-severe disability manifested through the inability to have an independent life (can not go without help, can't handle personal needs alone) but does not require permanent care, was appreciated at 8 (11, 94%) patients. Severe disability with bed immobility, requiring permanent day and night care, gr V, respectively, was determined in 2 (2,98%) patients. Note that grade VI, to whom death is attributed, was reported to a patient at the time of examination.

Table 2. **Consequences of idiopathic inflammatory myopathies (n = 67)**

Variable	**Nr patients, abs**	**Nr patients, %**
Disability according Rankin scale		
Gr I	21	31,34
Gr II	24	35,82
Gr III	11	16,42
Gr IV	8	11,94
Gr V	2	2,98
Gr VI	1	1,49
Prednisolon-equivalent dose		
<10 mg	18	26,86
≥10 mg	49	73,14
Activity	40	59,70
Remission		
Drug-induced	24	35,82
Without drugs	3	4,48
Heart involvement		
Synusal Tachycardia	7	10,45
Rythm disturbances	11	16,41
Vascular involvement		
Sindrom Raynaud	15	22,38
Livedo reticularis	4	5,97
Sjogren Sindrome	2	2,98
Antiphospholipidic Sindrome	7	10,45
Mechanic hands	2	2,98
Osteopenia	12	17,91
Headache	8	11,94
Prostate adenoma	2	2,98
Uterine mioma	7	10,45

Later we were interested to analyze Rankin's disability according to the duration of the disease (Figure 3).

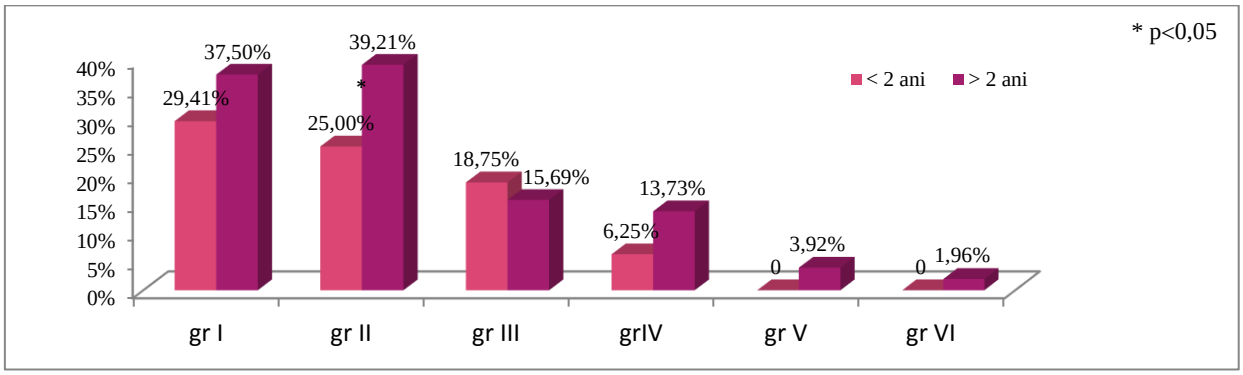


Figure 3. **Grades of disability according to the Rankin scale depending on the duration of the disease**

The data presented in figure 3 shows that patients with grade I prevailed in group II, which constituted 37,5% versus 29,41% in group I. It is noteworthy that in the second group predominated patients with degree II of disability in 39,21% of cases versus 25,00% in group I. Disability according to III was assessed in 18,75% and 15,69% cases, group I and II, respectively. It should be noted that Grade IV in group I was set at only 6,25% compared to 13,73% in group II and Grade V was determined in 6,25% of cases in the group with the duration of illness under 2 years and which the moment of examination was in the period of acute illness. Subsequently we continued the research by correlational analysis of the degree of disability with various variables of interest (table 3). Thus, moderate reverse correlation between Rankin scale disability and disease duration under 2 years ($r = -56$, $p = 0,02$) was identified.

Table 3. **Correlative analysis of disability depending on the duration of the disease**

	MMT-8	**MDGA**	**PGA**	**SF-8 MCS**	**SF-8 PCS**
Disease duration <2 years	R=0,80, p=0,002	R=0,54, p=0,02	R=0,51, p=0,04	R=0,35, p=0,1	R=0,52, p=0,03
Disease duration >2 years	R=-0,45, p<0,001	R=0,31, p=0,02	R=0,29, p=0,03	R=0,15, p=0,3	R=0,38, p<0,01

The data presented in the table indicates that for patients with less than 2 years of illness, reduced muscle strength is an important aspect, translated by the correlation between disability, MMT-8 scores, PGA and the physical quality of life component. Notable is that a moderate negative relationship was established between Rankin's degree of disability, and muscle strength assessed by MMT-8 in patients with a disease progression greater than 2 years, although no statistically significant correlation between Rankin's disability and duration disease. In this context, we note that administering the equivalent ≥10 mg of Prednisolone represented a risk factor for severe disability - RR 2,23; 95% CI from 1,34 to 3.69; $p = 0,002$, and the disease duration of less than 2 years was established as RR 0,44; 95% CI from 0,21 to 0,93; $p = 0,03$.

Another important aspect was the installation of clinical remission. To be noted that 30 (44,77%) patients with myopathy experienced remission, of which 24 (35,82%) were drug-controlled and 5 (7,46%) patients without medication. In addition, drug-controlled remission in the batch of the disease under 2 years of age was identified in 43,75%, and in group II in 33,33% cases. Regarding drug-free remission, 9.8% of patients in the group II were found in group II, patients in the age group under 2 years of age had no non-drug remission. In the context of those presented we were interested in studying the frequency of accidents in patients with idiopathic inflammatory myopathies. Thus, in the case of 40 (59,70%) patients, we determined that they were in the stage of acute illness, and the rate of flares in lot I was 1,33±0,65, and for lot II was calculated 2,27 ± 0,91 per patient. We then analyzed the dose of equivalent Prednisolone in the examined patients. Thus, we determined that in 18 (26,86%) patients the dose was < 10 mg and 49 (73,14%) was higher, including 10 mg.

Subsequently, we continued the research by determining the cardiac damage, manifested by sinus tachycardia in 7 (10,45%) cases and rhythm disturbances in 11 (16,41%) patients. Vascular involvement with Raynaud's syndrome was identified in 14 (20,89%) subjects, and livedo reticularis was present in 4 (5,97%) cases. Note that antiphospholipid syndrome was diagnosed in 2 (2,98%) subjects. As a consequence, mechanic hands was expressed in 7 (10,45%) patients. Another outcome of interest was Sjogren's syndrome detected in 2 (2,98%) patients with disease duration greater than 2 years. Continuing patient research, we found the presence of headache in 8 (11,94%) patients, of whom 2 (12,5%) of group I and 6 (11,76%) cases in group II.

It should be noted that 9 (13,43%) patients in the investigated group were diagnosed with benign tumor, manifested by prostate adenoma and uterine fibroids. Therefore, in lot I in 6.25 cases, uterine myoma was identified, prostate adenoma in 2 (3,92%) men and 6 (11,76) women were diagnosed with uterine myoma was determined in the group with disease duration greater than 2 years.

In accordance with the objectives and the vector of the researchers in the field, we continued the research by examining patients with IIM by musculoskeletal ultrasonography and nuclear magnetic resonance of soft tissues in the thighs. Research results have shown that USG data in patients with IIM can reveal a variety of manifestations that can characterize both the onset of the disease and its consequences, such as edema and muscle atrophy. Thus, in the study group, 38 patients were subjected to musculoskeletal ultrasonography, 20 of them had less than 2 years and 18 had a disease duration of more than 2 years (table 4).

Table 4. **Ultrasound changes detected in patients with idiopathic inflammatory myopathies**

Parameters	**IIM patients, n=38**	**IIM patients, %**
Decreased ecogenity	5	13,16
Increased ecogenity	10	26,32
Diffuse/localized edema	3	7,89
Muscle atrophy	19	50,0
Fasciitis	6	15,79
Hipervascularization	5	13,16

The data shown in the table show the presence of low ecogenity in 5 (13,16%) patients, of which 4 (25,0%) had a disease duration of less than 2 years and a subject lasting more than 2 years. Increased ecogenity was determined in 10 (26,32%) patients, 3 (15,0%) and 7 (38,89%) subjects in groups I and II, respectively. Thus, the incidence of focal or diffuse edema was found in 3 (7,89%) patients who had the disease duration of less than 2 years. I drew attention to a sign such as muscle atrophy, which was detected in 19 (50,0%) patients. Note that the decrease in volume of the ultrasound-confirmed muscle tissue was established in 3 (15,0%) patients in group I and 16 (88,89%) with disease duration greater than 2 years, which is explained by the interest of the primordial myopathic process. The presence of fasciitis, expressed by thickening of the fibrous septum dividing the muscle fascicles, was determined in the USG, which was determined in 6 (15,79%) patients, of which 2 (10,0%) cases from lot I and 4 (44,44%) subjects with disease duration greater than 2 years. In order to visualize hypervascularization, the Doppler effect was applied, to note that this signal was evaluated in 5 (13,16%) patients with myopathies.

Later on, we continued the analysis of the identified changes in MRI patients in soft tissue of thighs, performed in 10 patients with a disease duration of less than 2 years and in 6 patients over 2 years (table5).

Table 5.**Changes found in MRI in patients with idiopathic inflammatory myopathies**

Parameters	**IIM patients, n=12**	**IIM patients, %**
Diffuse/localized edema	5	31,25
Diffuse/localized atrophy	10	62,5
Muscle atrophy	3	18,75
Fasciitis	5	31,25

According to the data in table5 the presence of muscle edema on MRI was identified in 5 (31,25%) patients in the study group, out of which 4 (40,0%) subjects were established during the

first 2 years of the disease, and in one patient occurred after the 2-year term. Focal or diffuse muscular atrophy was found more robust after 2 years of illness, in 8 (80,0%) patients vs 2 (33,33%) cases with disease progression less than 2 years, respectively.

It should be noted that the replacement of muscle tissue with adipose tissue was found less frequently and occurred in 3 (18,75) patients with MII after 2 years of illness. According to the data found in the above table, fasciitis was documented in 5 (31,25%) patients, 3 of them (30,0%) with disease duration less than 24 months and 2 (33,33%) patients with more than 2 years.

In conclusion, we can state that modern imaging methods used to highlight muscle involvement play an important role and have become fundamental tools in the evaluation, diagnosis and monitoring of the patients with muscular diseases. The results of our study demonstrate that these methods are useful and promising and complement the assessment of disease status and lesions in patients with idiopathic inflammatory myopathies.

4.2. Quality of life in patients with idiopathic inflammatory myopathy

The quality of life is determined by multifactorial activity, being a specific action exerted on the patient, conditioned by age, sex, premorbid health and associated comorbidities, but also by the disease subtype, the activity and the duration of the illness, also the importance of the administered drugs. At the same time, an important role is played by intrinsic muscular factors in idiopathic inflammatory myopathies, autoimmune diseases in which skeletal muscles are primarily affected, but also other systems and organs are involved. As with other chronic diseases, these patients experience depression, anxiety, fatigue, and so an important aspect in the multidimensional assessment of patients with myopathies is the quality of life assessment proposed by the IMACS and OMERACT working groups. Investigating IIM patients through multiple questionnaires involves increased time when completing them, including for SF-36 administration. For easy-to-understand reasons, we chose to apply the shorter version of SF-36 and SF-8, but which includes the same main areas: physically and mentally, being a new and reliable clinical tool. Figure 4 shows the values of both SF-8 components of the patients in the study group.

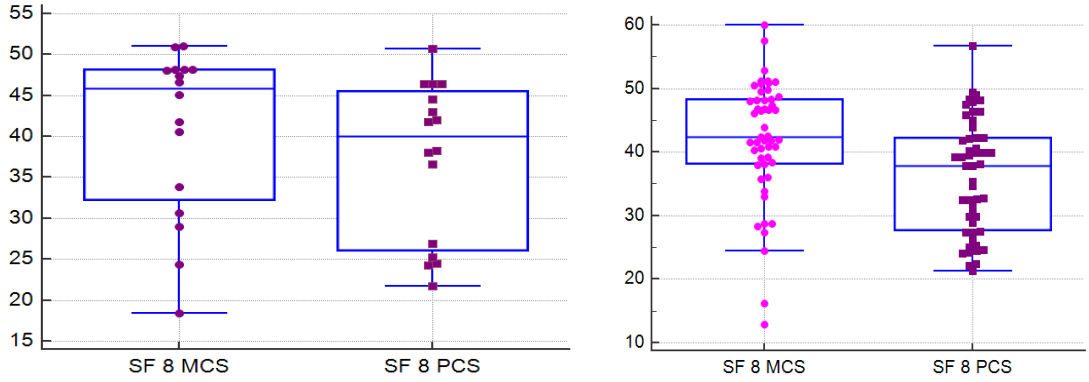


Figure 4**. Box-plot analysis of SF-8 values in patients in the study group depending on disease duration**

The data presented in the figure demonstrates the distribution of the quality of life values in relation to the average values, mentioning that these were less than 50, the physical and the mental component constituted 41,69 and 36,48, respectively, translated as low quality of life in myopathic patients, especially through the physical component. According to the data in the figure, the values of the mental component have a wider variation interval than the physical one.

We were further interested in analyzing the quality of life in patients with IIM depending on disease duration, 6-24 months and more than 2 years, results are shown in Table 6.

Table 6. The correlation of the quality of life with the duration of the disease

Disease duration	6-24 months	r	25 and more	r	P
SF-8 physic	37,30±9,63	0,53	36,23±8,94	0,24	<0,05
SF-8 mental	40,76±10,28	0,42	41,98±9,49	0,51	<0,05

Thus, we determined that MII patients in both groups bear more physical stress than the mental one, and the duration of the disease tends to influence the quality of life, so a moderate correlation (r = 0,49 p <0,05) between both areas of quality life and duration of illness up to 2 years, and in the group with a duration of more than 2 years we found a moderate correlation for the mental domain (r = 0,51 p <0,05) and a weak one for the physical one (r = 0,24 p <0,05). Note that we established a direct positive relationship between the physical component and the results of the manual muscular test, r = 0,53.

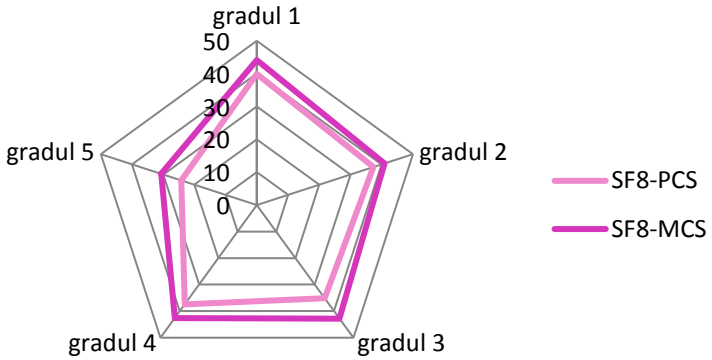


Figure 5. **The distribution of SF values depending on Rankin disability grades**

Given that the physical aspect is of major importance in the self-assessment of the quality of life in patients with myopathies, we considered it appropriate to analyze the SF-8 values depending on the degree of disability according to Rankin scale (Figure 5). Thus, according to the data shown in the figure, we can conclude that the quality of life, both by the physical and the mental component, tends to diminish with the aggravation of the patient's condition and his inability to be independent.

Subsequently we continued the research by identifying the variables of interest on the quality of life, so the impact items were plotted in figure 6.

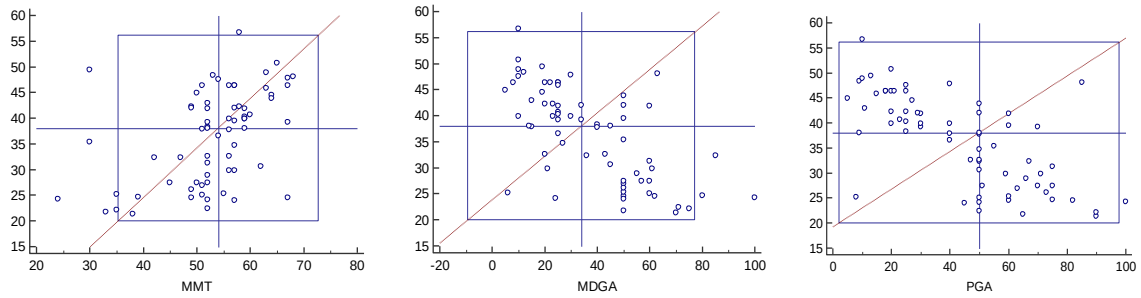


Figure 6. Correlative analysis of the physical component of the quality of life

According to the data presented in figure 6, we can say that the physical component of the quality of life determined by SF-8 in myopathic patients is inversely influenced by the activity of the disease determined by both the patient and the physician (r = -0,69; r = -0,65, p <0.0001), so high disease activity in turn leads to low quality of life in the physical domain. Also, it was determined a direct moderate correlation between physical element and muscle strength assessed by MMT-8 (r = 0,47, p <0,0001). Note that area of interest for the mental component was obtained

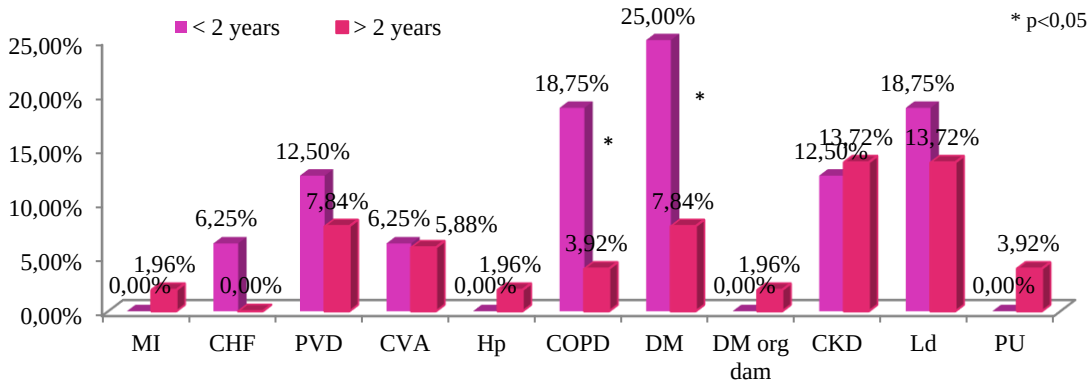
at an inverse relationship proportional to the disease activity determined by the patient, r = -0,44, p = 0,0002.

In conclusion, the quality of life of patients with idiopathic inflammatory myopathy is reduced primarily by the physical component and influenced by the disease activity.

4.3. Determination of comorbidities in patients with idiopathic inflammatory myopia

The above-mentioned data outlines the demographic status of patients with idiopathic inflammatory myopathy with an average age of 53 years in whom most of the general population have associated pathologies and which in turn can influence both disease progression and the quality of life of these patients. In the context of those mentioned, we considered it appropriate to determine the spectrum of comorbidities in the study group. Thus, in the investigated group we established an average value of 2.73±1.41 with an estimated survival rate of about 74 percentage points. It is worth mentioning that the rheumatologic affection, present in 100% of the investigated group, which is included in the ICC and the age of 50 years, increased ICC score from the start, and in the examined patients we identified a wide variation interval from 1 to 7, and the estimated survival rate fluctuated 0-96 percent. This diversity can be explained by the number of associated diseases in a patient. At the same time, we identified moderate inverse correlation between the estimated rate and the age of patients with myopathies at the time of examination (r = -0,67; p<0,0001), which emphasizes the importance of females in the development of comorbidities. Therefore, we intended to detect associated pathologies and their number in the patients in the study, so a single chronic disease in the concomitant disease series except IIM was established in 29 patients (43,28%), two and more pathologies associated patients were present at 8 (11,94%), and in 30 (44,78%) patients there were no concomitant diseases.

Next we intend to assess the most frequent comorbidities, in figure 7 there are presented the data obtained.



Note: *MI-myocardial infarction; CHF-chronic heart failure; PVD-peripheral vascular disease; CVA-cerebrovascular accident; Hp-hemiplegia; COPD-chronic obstructive pulmonary disease; DM diabetes mellitus; DM org dam-diabetes mellitus with organ damage; CKD-chronic kidney disease; Ld-liver disease; PU-peptic ulcer*

Figure 7. Frequency of comorbidities according to ICC in study group

According to the results of our study, the rate of pathologies associated with the studied group, diabetes mellitus was most frequently identified in 11,94% of patients, followed by chronic obstructive pulmonary disease – 7,46% and 5,97% of peripheral vascular disease and liver disease. Note that in the studied group no such diseases as AIDS, hematologic or metastatic malignancies or dementia were noted. Later we were interested in analyzing the age of the patients in the investigated group depending on the number of identified co-morbidities.

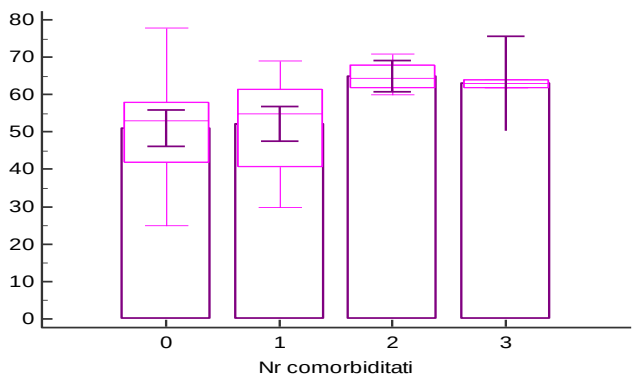


Figure 8. Box-plot analysis of comorbidities depending on the age of MII patients

The data shown in figure 8 shows that in the group of patients without comorbidities the age ranged from 25 to 78 years with an average of 51 ± 13,19 years. Regarding the age of subjects with concomitant disease, an average of 52,17 ± 11,95 years with a variation interval of 30 to 69 years was certified. A narrower range was observed in patients with myopathies with two or more associated diseases, so the age varied from 60 to 71 years, and the average cost was 64,5 ± 3,55 years.

4.4. The medical-social impact of idiopathic inflammatory myopathies

In accordance with the set out tasks, I considered it appropriate to study the patients' satisfaction with the medical services provided. From the perspective of these, we have used Patient Satisfaction Questionnaire III (PSQ III) which is a generic tool for satisfaction assessment and encompasses 7 domains. The data obtained by the application of PSQ III were analyzed by comparing with the minimum, maximum, average in the general population, in 2 lots after the disease duration: group I - less than 2 years, early myopathies and group II - more than 2 years, illness installed. The scores obtained in the general satisfaction score in the group I was 19,19 ± 3,19 points and in lot 2 – 18,73 ± 2,77 points, statistically insignificant difference ($p > 0,05$). We collated the data obtained on the basis of our survey, with the average PSQ-III average population. At the same time, we took into account the minimum and maximum values resulting from the study and we confronted with the PSQ-III values. Study results assumed 14 and 24 points, and PSQ-III assumed 10 and 50 points, respectively. We continued the research in the same way. Regarding the technical quality, the average scores obtained were 36,44 ± 5,23 (i-v 32-49 points) for lot I and 34,14 ± 5,21 (i-v 21-49) for group II. The results in both groups compared with the mean of PSQ-III, which constituted 30 points, the satisfaction of the patients with the technical quality in the early MII group was higher compared to the patients with the disease but also to the PSQ-III average. We were interested in the comparative analysis of the individual relationships, which implied that in the interpersonal aspects the highest average score was presented by patients in lot II and lot I, which represents 25,06 ± 3,64 (iv. 17-34) points and 24,31 ± 4,80 (iv. 19-33 points), respectively. The comparison of the obtained results with the average in the general population reveals indicators below, which represented 21 points. We continued by estimating "communication" and we recorded 18,13 ± 3,9 and 18,53 ± 3,64 respectively lot I and II compared to only 15 points in the general population. In this context, we analyzed patients satisfaction with the time spent with the doctor, who scored higher in the second group compared to the first group and the average in the general population (6, 6,44, 6,49 points) with the values for the group. The results of the "communication" field were related to "interpersonal aspects" ($r = 0,76$, $p<0,05$), which means the effective degree of doctor-patient communication in the study group. Partial

dissatisfaction with the time spent with the doctor was due, on the one hand, to the length of the medical consultation, the investigated patients stated that the conversation with the doctor lasted more than 20 minutes, on the average in the examined group was 24,03 ± 6,23 with a range of 20 to 40 minutes).

On the field of "financial aspect", the results obtained in patients with idiopathic inflammatory myopathies revealed a lower level of satisfaction than the average score in the general population which is estimated in the average at 24 points. Concerning the patients with disease under 2 years, the financial satisfaction was only 20,75 ± 4,61 points and for the ones with an evolution of more than 2 years – 20,94 ± 4,59 points, which is explained in terms of both the reduced income due to disease manifestations - disability and sickness costs. According to the PSQ-III methodology, financial satisfaction is wide range from 8 to 40 points. We reiterate that our own data was below the expected average of about 20 points. Of particular interest was the section on access, comfort and availability of medical services, with primary care in the context of primary health care, referring to the family doctor. According to the obtained data, the satisfaction in this field is higher in lot II followed by lot I, noting that the average in the general population constituted 36 points. We reiterate that the minimum and maximum score was 12 and 60 points. Thus, the results obtained accounted for 70% of the availability of the medical assistance expected by the patient.

When applying PSQ-III, we determined that patients with idiopathic inflammatory myopia had a general satisfaction level slightly above the average of the general population. Thus, in the group with duration of illness less than 2 years, general satisfaction showed a direct and close correlation with the field of "communication", but also with "time spent with the doctor" ($r = 0,9$, $r = 0,8$ $p < 0,05$). Also, patients are satisfied in the areas of technical quality, communication, interpersonal aspects and access / comfort / availability, between them being a direct, close relationship, demonstrated by $r = 0,89$, $r = 0,76$, $r = 0,8$, $p < 0,05$. Although patients in the group with disease duration more than 2 years of age have a higher degree of satisfaction in the same areas as those in group I, the correlations between domains slightly differ, a positive relationship has been established between access / comfort / availability and overall satisfaction, technical quality and communication ($r = 0,72$, $r = 0,73$, $r = 0,66$, $p<0,05$), indicating that the convenience prevails for these patients. However, the investigated patients are less satisfied with the financial aspect, which is due to the need for various, and expensive medical services, given the specificity of the pathology. The importance of determining the patient satisfaction makes it possible to focus on the assessment of medical services from a patient perspective, which can help improve the quality of provided health services, and assess the attitude towards the financial aspects of health care.

In the context of assessing the medical and social impact, we continued the research by determining the type of employment (figure 9).

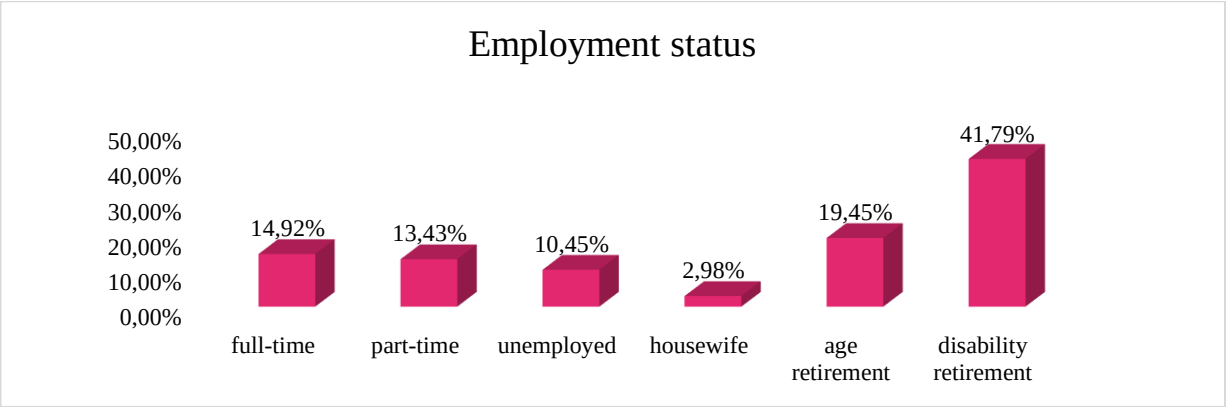


Figure 9. **Employment status in idiopathic inflammatory myopathies patients**

According to the data presented in figure 9 above, there were 19 (28,35%) employed patients in the study group at the time of the study, they additionally completed the WPAI-GH Questionnaire regarding the last 7 days. Analysis of patient responses found that patients were absent from work during the last week from 0 to 35 hours, representing 0-86,5% of working hours (absenteeism) with an average of 17,06 ± 4,7%. At the same time, the presence at work - the loss of productivity in hours at work was 26,47 ± 9,3% with varying ranges from 0 to 28 hours, which makes up 0-70% of cases. The loss of overall productivity was 36,19 ± 28,09 (i-v 1-93,25%) percent cases. Regarding the field of activity limitation outside of the service, it was 28,82 ± 22,33% with a variation interval of 0 to 80% of cases.

We redirected the research vector to the degree of correlation of WPAI components with various variables of interest, so we determined that the MMT-8 muscle strength correlates moderately with absenteeism, $r = 0,46$, $p<0,05$. The important influence of the autoimmune process in myopathy on the employed is translates into increased absenteeism, presence, and low productivity, which implies a lower performance both at work and in daily activities. The results of our study revealed that only 28,35% of the surveyed group ware employed, full-time or part-time, the average of presenteism constituting 26,47% of cases, partly by the performance of work, coupled with low labor productivity.

Chapter 5 is a compartment of analysis and reasoned deliberations on the own investigations results by assessing the consequences of patients with IIM, both within the general group and as a function of the duration of the disease, and interpreted the clinical evaluation data.

Following the analysis of the obtained results, we developed an evaluation scheme for patients with idiopathic inflammatory myopathies (Figure 10).

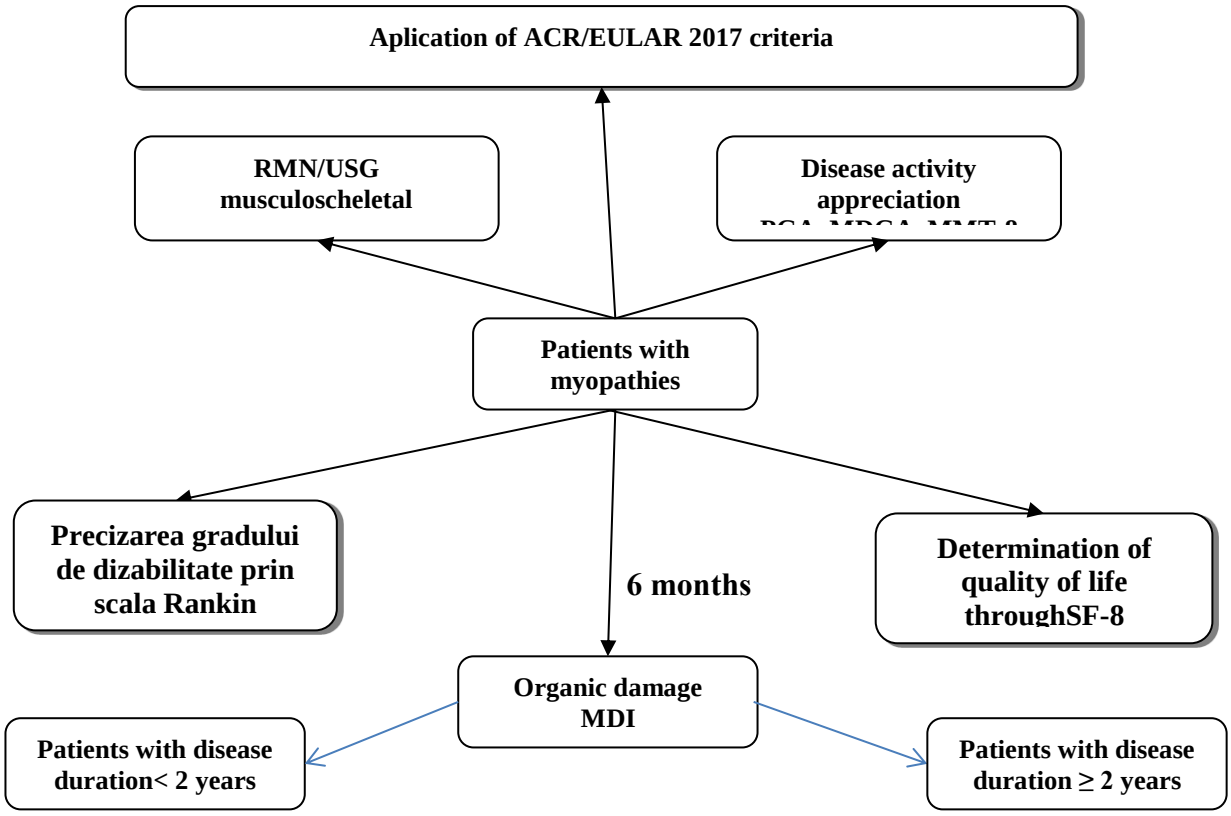


Figure 10. **The approach model of patients with idiopathic inflammatory myopathies**

GENERAL CONCLUSIONS AND RECOMMENDATIONS

GENERAL CONCLUSIONS

1. The study highlighted that the assessment of patients with idiopathic inflammatory myopathies by the new classification criteria ACR / EULAR facilitated the diagnosis, 7,52±2,21 criteria were evaluated in the study group and outlined their usefulness

2. The assessment of the disease outcomes revealed that in the patients with disease duration up to 2 years were found as more frequent: muscular dysfunction – 87,5%, dyslipidemia – 37,5%, dysphagia – 31,25% and 25,0% - arterial hypertension, despite moderate activity of the disease, when during the course of the disease, more prevalent was osteoporosis – 62,74%, alopecia – 25,94% and dysphagia – 52,94%

3. The results of the research determined the decrease of the quality of life of the patients mainly through the physical component (36,48 points) versus the mental one (41,69 points). In patients in the disease duration less than 2 years, both areas of quality of life were influenced by the duration of the disease ($r = 0,49$, $r = 0,51$ $p < 0,05$), whereas in the group with disease duration more than 2 years , moderate correlation with the mental domain was determined ($r = 0,51$ $p < 0,05$)

4. The results of the research found low work productivity through increased presenteeism-82,94 ± 4,7%, absenteeism-26,47 ± 9,3% and low overall productivity-36,19 ± 28,09% cases.

5. Patient`s satisfaction appreciated by PSQ-III was increased in the access, comfort and availability of healthcare domain, meanwhile diminished satisfaction was in the field of financial issues and time spent with the doctor.

6. According to the results of the study, in the group with disease duration less than 2 years frequent comorbidities were diabetes in 25,0% of patients, chronic obstructive pulmonary disease – 18,75% and in group with disease duration more than 2 years renal disease was detected in 13,73% and hepatic disease at 11,76 % cases. Estimated survival rate at 10 years in patients with disease duration less than 2 years was 70,1%, and in patients with disease duration more than 2 years -74,5 % cases

PRACTICAL RECOMMENDATIONS

1. It is necessary to apply the ACR / EULAR 2017 classification criteria by rheumatologists to patients with specific / suggestive clinical signs of myopathies

2. For the purpose of early identification of the disease outcomes, patients with idiopathic inflammatory myopathies should be investigated multidimensionally, by applying myositis damage index, after 6 months of illness, including up to 2 years,

3. In the subsequent CNP-319 review to complete mandatory investigations for ambulatory and hospital care including the musculoskeletal USG, MRI

4. Personalized approach and schooling of the idiopathic inflammatory myopathy patient in order to maintain remission, and at the occurrence of suggestive signs of the disease outcomes to early doctor addressing.

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- **articles in ISI, SCOPUS and other international databases ***

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