

REVISED EDITION OF A TEXT

on dissertation work on the procedure for obtaining the educational and scientific degree
"DOCTOR"

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Topic of the dissertation: "Determinants of quality of life in patients with non-radiographic axial spondylarthritis: an analysis based on the main aspects of the disease"

Reviewer: Prof. Dr. Nikolay Yordanov Penkov, MD

The dissertation of *Dr. Svetoslav Dimitrov* examines a current problem in modern rheumatology - "Determinants of quality of life in patients with non-radiographic axial spondylarthritis and makes an analysis based on the main aspects of the disease. Axial spondylarthritis (axSpA) is a chronic inflammation of the sacroiliac joints and parts of the spine. The term includes the classic inflammatory joint disease - ankylosing spondylitis (AC), as well as non-radiographic axial spondylarthritis (nr-axSpA). The lack of radiographic evidence of structural changes in the sacroiliac joints distinguishes the two conditions. However, in both groups of patients, magnetic resonance imaging (MRI) revealed inflammatory changes in the sacroiliac joints, which with the progression of the disease process lead to irreversible structural changes. It is known that the quality of life is impaired in almost all rheumatic diseases. This also applies to patients with non-X-ray axial spondylarthritis. The progression of structural changes in these patients correlates with a progressive deterioration in their quality of life. That is why it is

very important to know the factors that worsen the inflammatory and structural changes in the joints and change the quality of life accordingly.

Dr. Dimitrov's dissertation is the result of a well-planned clinical trial. The examination of the patients was realized in the Clinic of Rheumatology of the University Hospital "St. Marina EAD - Varna in cooperation with the Clinical Laboratory and the Department of Radiology.

The dissertation is written on 158 standard pages and is illustrated with 35 figures, 40 tables and 14 appendices.

The literature is based on 202 titles - all in Latin, and most of them published in the last 10 years. It is noteworthy that two of the literature sources (№ 1 and № 2) are included in the list of reports related to the dissertation. This is not allowed and there is no logic. The literature review is well structured. The modern concept of spondylarthritis is considered and the evolution of clinical thinking over time is traced. The frequency of AS and its variations depending on the geographical regions and the different distribution of HLA-B27 are shown. An overview of the clinical symptoms of spondyloarthritis has been made. The role of the inflammatory type of spinal pain in the diagnosis of ankylosing spondylitis is emphasized. The development of non-radiographic axial spondylarthritis was monitored. The similarities and differences between ankylosing spondylitis and nr-axSpA are discussed. Gender differences in nr-axSpA are shown. The methods for estimating nr-axSpA recommended by ASAS are discussed. The role of figurative methods for the diagnosis of sacroiliitis has been described propaedeutically. Particular attention is paid to the MRI criteria. Particular attention is paid to how and to what extent nr-axSpA changes the quality of life in patients. An overview of the treatment and its effectiveness in patients with nr-axSpA has been made. Finally, the unresolved and controversial issues in this disease state are presented.

Aim and tasks of the study:

The aim of the dissertation is logically derived from the unresolved and controversial issues in the literature review and is defined precisely and clearly. The total number of tasks 7 specifies the ways to achieve the set goal.

Clinical material and research methods:

After screening according to the ASAS questionnaire to prove or exclude inflammatory spinal pain and a study with pre-selected methods, 202 patients were included in the study. They are divided into 3 groups - nr-axSpA arm (n = 98), nr-axSpA arm (n = 62) and control group (n = 42).

The research methods include: questionnaire for including and excluding criteria, methods and means for proving the disease activity, anamnesis, physical status, assessment of spinal mobility by - BASMI, examination of the peripheral joints, search for ocular symptoms.

Also used: clinical indices for disease activity, assessment of the severity of functional disorders in patients with SpA, assessment of quality of life in patients with nr-axSpA, assessment of inflammation of the sacroiliac joints using magnetic resonance scoring system - SPARCC and SPARCC minus and ESR and C-reactive protein were tested.

The statistical analysis of the obtained results is wide and allows methods that allow for an accurate assessment of their significance.

Results and discussion:

The mean age of the three study groups and the sex distribution of the whole nr-axSpA group and the control group did not differ. The duration of the disease process in the control group is significantly greater than that of the whole group with nr-axSpA. The mean values of ESR and C-reactive protein in patients with the imaging arm are significantly higher than those in the clinical arm, and in patients in the control group significantly lower than in the first two groups. There is a positive correlation between laboratory biomarkers and clinical indices for the assessment of disease and functional impairment in patients with nr-axSpA. This speaks of the great diagnostic informativeness of these indices and their importance for clinical practice. Changes in the sacroiliac joints detected by magnetic resonance imaging show a strong correlation with markers of inflammation and scores for assessing disease activity in patients with nr-axSpA imaging arm. Non-radiographic axial spondylarthritis limits physical activity. Functional disorders are more severe in patients who have and spinal symptoms - peripheral arthritis or enthesitis. Restrictions on spinal motility in patients with nr-axSpA are significantly more severe than in the control group. The imaging arm in the studied patients showed statistically significantly more severe axial damage compared to the clinical arm. The quality of life in patients with nr-axSpA is worse than in the control group and is directly correlated with laboratory markers of inflammation and indices for assessing disease activity. There is no significant difference in the quality of life of patients with imaging and clinical shoulder. The mean values of acute-phased reactants and ASDAS-CRP in men with nr-axSpA are significantly higher than in women.

Physical function, quality of life and SPARCC do not differ between the sexes. Non-steroidal anti-inflammatory drugs and sulfasalazine have no effect on disease activity and physical activity in patients with nr-axSpA. Smoking impairs the quality of life in patients with non-radiographic axial spondylarthritis.

Conclusions:

The aim of the dissertation is fulfilled. The conclusions are 8 in number and correspond precisely and clearly to the set tasks.

Contributions to the dissertation:

Dr. Dimitrov's research is original and confirmatory. For the first time in our country it has been analyzed - the demographic characteristics, the laboratory constellation, the disease activity, the motor deficit and the quality of life in patients with non-radiographic axial spondylarthritis. A comparative analysis of the imaging and clinical shoulder was performed in patients with non-radiographic axial spondylarthritis. A comparative analysis was performed by sex both in the general group and by subgroups in patients with non-X-ray axial spondylarthritis. A link between the SPARCC scoring system and the level of overall disease activity and quality of life in patients with non-radiographic axial spondylarthritis has been established. A simplified algorithm of daily medical practice for early diagnosis of SpA before its radiographic phase has been proposed. It has been confirmed that in patients with nr-axSpA with a short duration of symptoms and in the absence of irreversible structural changes, quality of life may be poor. The sex distribution of patients with nr-ax SpA does not differ, and the disease activity in men is higher. There is a connection between the acute phase indicators and the levels of the disease process. It has been confirmed that the levels of disease activity according to ASDAS-CRP in patients with extraaxial manifestations are higher.

The abstract of the dissertation has a standard structure and very accurately summarizes the dissertation.

Publications and participation in scientific forums:

Dr. Dimitrov has made 7 scientific papers in connection with the dissertation - 4 published in journals and 3 presented at conferences and symposia.

CONCLUSION:

An interesting scientific development, treating a topical and insufficiently studied problem in our country. The literary review has scientific merits and can serve as a reference on the topic. The purpose of the dissertation and the tasks for its realization are defined precisely and clearly. The clinical material is sufficient for the realization of the set goal and tasks. The research methods are modern and informative enough. The results obtained enrich the clinical knowledge on the problem of nr-axSpA and show that the most important for the evolution and results of treatment of these patients is early diagnosis. The quality of life in nr-axSpA as in all other rheumatic diseases is impaired. This is directly dependent on laboratory biomarkers of inflammation, indices for assessing disease activity and the severity of structural changes detected by imaging diagnostic methods. The author proposed a simplified algorithm for early diagnosis before the radiographic phase of SpA. It can be said with full conviction that the purpose of the dissertation has been fulfilled. The conclusions in total 8 correspond exactly to the set tasks. The dissertation of Dr. Dimitrov is contributing and confirmatory. Fully meets the requirements for awarding the educational and scientific degree "DOCTOR". That is why this gives me reason to suggest to the members of the scientific jury that they vote in favor.

June 25, 2022

Varna

REVIEWER

(Prof. Dr. Nikolay Penkov, MD)