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Neuropsychological manifestations in rheumatic patients with chronic pain

Неуропсихолошке манифестације код реуматолошких болесника са хроничним болом

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SUMMARY

Introduction/Objective Patients with rheumatoid arthritis (RA), osteoarthritis and fibromyalgia, alongside chronic pain, often suffer from functional disabilities, as well as cognitive dysfunction.

The aim of this study is to compare the intensity of pain, symptoms of depression, anxiety, and memory ability among rheumatic patients with chronic pain and to compare rheumatic patients to a control group of healthy participants.

Methods The cross-sectional study, which included 110 (82 women; 28 males) patients with chronic pain, was done at the Special Hospital for Rheumatic Diseases, Novi Sad. Depression was determined by Beck's Depression Inventory, anxiety was diagnosed by Spielberger's anxiety test and memory was assessed by the Wechsler Memory Scale.

Results Mean pain intensity in patients with fibromyalgia were statistically significantly higher compared to patients with osteoarthritis and RA ($p < 0.05$). A statistically significant difference in the psychological status of patients ($p < 0.001$) and patient memory ($p < 0.05$) with chronic pain was established, compared to patients in the control group. There was no statistically significant difference in the psychological status of patients, patient memory level and pain intensity in patients with positive fibromyalgia test results in comparison to rheumatic patients not meeting the criteria for fibromyalgia. Patients with osteoarthritis had a statistically significantly lower memory coefficient in comparison to patients with RA and fibromyalgia.

Conclusion In RA, osteoarthritis, and fibromyalgia patients, clinical factors such as pain, depression, and anxiety play an active role in cognitive impairment and should be considered when planning treatment.

Keywords: chronic pain; rheumatic diseases; emotions; memory

САЖЕТАК

Увод/Циљ Пацијенти са реуматоидним артритисом, остеоартритисом и фибромијалгијом имају често поред хроничног бола, функционалну онеспособљеност, као и когнитивне дисфункције.

Циљ рада је био поређење интензитета бола, симптома депресије, анксиозности и способности памћења између пацијената са реуматским болестима и хроничним болом, као и да се упореде пацијенти са реуматским болестима и контролна група здравих испитаника.

Методе Студија пресека у коју је укључено 110 (82 жена, 28 мушкараца) болесника са хроничним болом је спроведена у Специјалној болници за реуматске болести у Новом Саду. Депресија је процењивана применом Бекове скале, анксиозност коришћењем Спилбергеровог упитника, меморија применом Векслерове скале меморије.

Резултати Средње вредности интензитета бола код пацијената са фибромијалгијом, су биле статистички значајно више у односу на пацијенте са остеоартритисом и реуматоидним артритисом (РА) ($p < 0,05$). Статистички значајна разлика у психолошком статусу пацијената ($p < 0,001$) и меморији пацијента ($p < 0,05$) са хроничним болом је показана, у поређењу са контролном групом. Није било статистички значајне разлике у психолошком статусу пацијената, нивоу меморије пацијента и интензитета бола код пацијената са секундарном фибромијалгијом у односу на пацијенте са РА који не испуњавају критеријуме за фибромијалгију. Пацијенти са остеоартритисом су имали статистички значајно нижи коефицијент меморије у односу на пацијенте са РА и фибромијалгијом.

Закључак Код пацијената са РА, остеоартритисом, и фибромијалгијом, клинички фактори као што су бол, депресија и анксиозност играју значајну улогу у когнитивним поремећајима, те би на то требало обратити пажњу при планирању лечења.

Кључне речи: хронични бол; реуматске болести; емоције; меморија

INTRODUCTION

Pain is an unpleasant and complex sensory and emotional experience [1]. A mutual interaction between pain and cognitive processing was determined [1]. Pain impairs cognitive functioning, while cognitive functioning may reduce the level of pain perception [1].

Chronic pain and depressive symptoms are often associated clinically, and together they make treating patients difficult. Depressive symptoms could prolong duration of pain as well as increase the intensity of pain [2].

Depression and anxiety are psychiatric disorders which could be associated with rheumatoid arthritis (RA), osteoarthritis (OA), and fibromyalgia (FA). The explanation for this association could be a biological, possibly cytokine-related, or it can be explained by prolonged negative impact of medical condition on mental health of patient [3].

Cognitive impairment is defined by memory loss, difficulties in learning new things, solving problems, decision making or problems with concentration. There is evidence that RA influences cognitive processing [4].

Patients with chronic pain and FM have deficits in working memory [5].

Several studies shown the high level of affective disorders in patients with chronic pain [6]. Severe depression is prevalent among patients with chronic pain. With the development of pain into a chronic condition, disorders such as anxiety, anhedonia, sleep disorders, cognitive impairments, and suicide may occur along with negative emotional states [6].

Pain, anxiety, and depression may impair work ability in different chronic rheumatic diseases [7]. There is association of chronic pain and neurocognitive impairment [7]. The pain may cause an emotional distress, which also contribute to reduce patient ability to cope with chronic pain self-management as well as with global functioning [7]. However, it is not easy to define the relationship between pain and neurocognitive impairment. There is possibility that pain could cause cognitive impairment or vice versa, that cognitive impairment is associated with higher risk of chronic pain. [7]

The challenges of chronic disease could potentially be decreased, and patient-oriented care could be improved by interventions focused on the symptoms. To adequately inform clinical practice, additional studies of treatment interventions are necessary. Continued workplace engagement in patients with chronic health conditions could be supported by further improvement of workplace accommodation and other such interventions [8].

METHODS

The study included 110 (40 with RA, 40 with OA, 30 with secondary FM) (82 female, 28 male) patients with chronic pain. The control group consisted of 30 healthy subjects (CO

group). The research was started in April of 2021 and finished in November of 2021, in the Special Hospital for Rheumatic Diseases, Novi Sad. RA group satisfied the criteria for the diagnosis of RA of American College of Rheumatology Association (2010 ACR/EULAR criteria) [9], FM group met the modified ACR criteria [10], and OA group met ACR criteria [11, 12, 13]. Exclusion criteria were: neurological and psychiatric diseases, hearing impairment, dementia, head trauma, any use of psychoactive substances and antidepressants at least a month before the study. The data from history, clinical examination, and questionnaires were used in study. The following parameters were collected in RA group: joint pain defined by a visual analogue scale (VAS) of 0-100 mm, painful and swollen joint count, erythrocyte sedimentation rate, and Disease Activity Score (DAS 28) which divided patients in two groups (RA-MDA Medium Disease activity - DAS 28 > 3.2 < 5.1; and RA-HDA (High Disease activity - DAS 28 > 5.1). The test for evaluation of emotional manifestations, Spielberger's anxiety test (Spielberger Trait Anxiety Inventory State and Trait), was applied for determination of anxiety, that includes questionnaires STAI-S and STAI-T for standardized measurement of current and general anxiety. A score below or equal to 30 points defines a low level of anxiety, while a score of 31-44 indicates a moderate level and a score above 45 represents a high level of anxiety. Beck's depression scale (Beck's Depression Inventory-BDI) was used for evaluation of depression. BDI total score defines the severity of depression. The scores above 30 imply severe clinical depression. Wechsler Memory Scale (WBsp Form 1) was used to detect verbal and non-verbal memory functioning with correction for the age group.

The study has been approved by the Ethics Committee of the Special Hospital for Rheumatic diseases, Novi Sad, Serbia (ethical approval number 14/28-5/1-21).

Statistical methods

The descriptive statistics measures were applied as follows: mean, frequency, measures of variation. Parametric (student t-test) and nonparametric (Mann-Whitney test, chi-square test) were used to compare two groups. The analysis of variance ANOVA and Kruskal-Wallis test was used to compare three or more groups. Pearson correlation coefficient was used for correlation of continuous variables.

RESULTS

There were 40 patients with RA (26 RA-MDA; 14 RA-HAD), 40 patients in OA group, and 30 patients in FM group, as well as the control group that was made of 30 subjects of good health (CO group) who had no significant age difference in comparison to chronic pain groups (CV < 30) (Table 1). The average pain intensity values determined using VAS scales were statistically significantly higher in patients with FM than patients with RA and patients with degenerative disorders (Table 1).

Average depression score assessed by BDI was in the CO group 7.41 ± 0.84, in the RA MDA group 16.39 ± 12.65, RA HDA 19.13 ± 10.25, OA group-12.72 ± 8.4, FM group 18.18 ± 12.61 (Table 2). There was statistically significant difference of depression scores between all 3 groups and the control group ($p < 0.001$) (Table 2), and a statistically significant difference of the depression scores between FM, RA-HDA, RA-MDA and OA group ($p < 0.05$) (Table 2).

Average state anxiety score assessed by STAI-S test was 41.63 ± 7.83 in the CO group, 52.25 ± 5.66 in RA-MDA group, 55.17 ± 5.01 in RA-HDA group, 53.12 ± 6.94 in OA group, and 54.68 ± 6.34 in the FM group. Statistically significant difference in state anxiety scores were found between all three groups and the control group ($p < 0.001$) (Table 2). However, no statistically significant difference in state anxiety scores were detected between the groups of patients with chronic pain (Table 2).

Average general anxiety score by STAI-T test was 40.73 ± 8.01 in CO group, 49.06 ± 6.86 in RA-MDA group, 50.04 ± 6.84 in RA-HDA group, 49.15 ± 6.24 in OA group, 49.32 ± 6.57 in the FM group. Statistically significant difference of general anxiety scores was found between the control group and all three groups of patients with chronic pain ($p \leq 0.001$) (Table 2).

The results of the STAI-S test differ in patients with RA grouped against DAS 28 disease activity (RA-MDA, DAS 28 ≥3.2 < 5.1; RA-HAD, DAS28>5.1), and no differences in BDI, STAI-T, WMS in relation to activity of the disease in patients with RA were found (Table 2).

There was a statistically significant difference in memory coefficients using the Wechsler Memory Scale between RA patients (RA-MDA-125.11 ± 14.18, RA-HDA 124.08 ± 13.03, OA group 108.95 ± 19.05, FM 123.75 ± 15.39) and healthy controls (136.37 ± 6.06) (RA *vs.* CO $p < 0.05$; FM *vs.* CO $p < 0.05$), (OA *vs.* CO $p<0.001$). The statistically significant lower memory values were present in OA group comparing with RA and FM group ($p < 0.001$).

DISCUSSION

Our results showed the highest depression score (BDI) and current and general anxiety score (STAI -S / STAI-T) in patients with rheumatoid arthritis (RA-HDA), and the lowest BDI score in patients with OA.

Patients with RA have a high prevalence of psychiatric comorbidities, which aligns with our findings. The lifetime prevalence of depression is estimated to be 41–66%, and for anxiety disorders is up to 70% [14, 15, 16].

By examining the differences in the degree of anxiety and depression of patients with RA and the control group, a statistically significant difference was established in the coefficients of depression among people with RA (BDI, RA-MDA-16.39 ± 12.65, RA-HAD-19.13 ± 10.25) and control group (6.93 ± 4.49) ($p < 0.001$), as well as in instantaneous scores (STAI-S) and general anxiety (STAI-T) ($p < 0.001$), which is in accordance with the literature data [17, 18].

Ozcetin and colleagues compared patients with RA, fibromyalgia and knee osteoarthritis in regards to anxiety and depression, and found the highest average BDI score in FM patients and the lowest in patients with OA knee, the lowest values of anxiety in FM, and the highest in RA [19].

Fibromyalgia often coexists with RA, which we can see in our results. Of the 30 patients with a positive test for FM, 25 (83.33%) already have a diagnosis of RA. These results are confirmed by the research of Frederick Wolf and his associates, which indicate a significant prevalence of FM and FM associate findings in patients with RA [20].

We established statistically significantly higher scores for anxiety and depression as well as the lower values of memory coefficients in people with FM compared to the control group of healthy subjects, which was found in previous studies [21, 22]. Cognitive impairment was found in patients with fibromyalgia compared with healthy controls, and the level of emotional disorders (depression and anxiety) may explain the heterogeneity of studies [23]. Additionally, data from the literature indicates that most patients with FM who have anxiety and depression also have poor quality of life and do not have adequate social support [24].

Our study did not establish a statistically significant difference in the psychological status of patients (depression, current and general anxiety of patients), patient memory level and intensity of pain in patients with positive FM test results in comparison to patients with rheumatic diseases who do not meet the criteria for FM. On the contrary, findings of Katz and associates found that in patients with FM there are more incidences of memory impairment

(70.2–24.6%), mental confusion (56.1–12.3%) and speech difficulty (40.4–3.5%), compared to patients with rheumatic diseases who do not meet the criteria for FM [24].

Our results also showed statistically significantly lower values of memory coefficients in patients with chronic pain (RA *vs.* CO $p < 0.05$), (OA *vs.* CO $p < 0.001$), (FM *vs.* CO $p < 0.05$) compared to the control group. The previous study on cognitive impairment in patients with RA compared to healthy subjects indicates a higher incidence of the presence of memory problems in patients with RA [25]. Furthermore, Roldán-Tapia and colleagues have shown that patients with RA and FM developed substantial cognitive impairments, which could not be easily explained by the pathology of this chronic diseases [26].

Our results have shown that patients with OA had statistically significantly lower memory values than patients with RA and FM. The association between memory loss and OA, is not fully explored. OA and joint pain were clearly linked with memory loss. The sleep and mood disorders could be associated with memory loss [27].

Pain has an immense impact on functional capacity and quality of life in patients with knee OA. The focus of the assessment should not be solely on the afflicted organ, but rather, importance should be given to functional disorders (physical, emotional, social) which patients may experience because of their illness [28].

The link between FM and depressive disorders could be the similarity of symptoms, like sleep problems and fatigue and shared biological and psychological mechanisms [29].

It is likely that depression in patients with RA is not only a consequence of the distress and disability caused by RA, but also contributed to by immunological changes. Targeting immunological pathways can, therefore, be used to lessen the mental burden in addition to treating rheumatoid arthritis. Regardless of immunological intervention, multidisciplinary approach including the psychiatrist and psychologist support is important in successful disease management [30]. Chronic pain is responsible for making patients more susceptible to mood disorders that can further deteriorate the perception, intensity, and duration of nociception, thereby making treatment and diagnosis more challenging [31]. Studies have shown that a genetic predisposition to chronic pain is linked to increased risk of depression [32].

CONCLUSION

Our study established a significant difference in the psychological status of patients (depression, anxiety) and the level of memory in patients with chronic pain (RA, OA, FM)

compared to the control group. Patients with FM had more intense pain compared to patients with OA and RA. Patients with OA had significantly lower memory coefficient values, as well as significantly lower average BDI values compared to patients with RA and FM. These results should be incorporated into the treatment approaches of such chronic and debilitating conditions. Longitudinal studies are required to confirm the cross-sectional findings.

Conflict of interest: None declared.

REFERENCES

1. Mazza S, Frot M, Rey AE. A comprehensive literature review of chronic pain and memory. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2018 Dec 20; 87:183-92. DOI: 10.1016/j.pnpbp.2017.08.006. PMID: 28797640.
2. Zhou W, Jin Y, Meng Q, Zhu X, Bai T, Tian Y, et al. A neural circuit for comorbid depressive symptoms in chronic pain. Nat Neurosci. 2019 Oct;22 (10):1649-58. DOI: 10.1038/s41593-019-0468-2. PMID: 31451801.
3. Lwin MN, Serhal L, Holroyd C, Edwards CJ. Rheumatoid Arthritis: The Impact of Mental Health on Disease: A Narrative Review. Rheumatol Ther. 2020 Sep;7(3):457-71. DOI:10.1007/s40744-020-00217-4.
4. Chaurasia N, Singh A, Singh IL, Singh T, Tiwari T. Cognitive dysfunction in patients of rheumatoid arthritis. J Family Med Prim Care. 2020 May 31;9(5):2219-2225. DOI: 10.4103/jfmpc.jfmpc_307_20. PMID: 32754477.
5. Castel A, Cascón-Pereira R, Boada S. Memory complaints and cognitive performance in fibromyalgia and chronic pain: The key role of depression. Scand J Psychol. 2021 Jun;62(3):328-338. DOI: 10.1111/sjop.12706. PMID: 33538343.
6. Yang S, Chang MC. Chronic Pain: Structural and Functional Changes in Brain Structures and Associated Negative Affective States. International Journal of Molecular Sciences. 2019 Jan; 20(13):3130. DOI: 10.3390/ijms20133130.
7. Higgins DM, Martin AM, Baker DG, Vasterling JJ, Risbrough V. The Relationship Between Chronic Pain and Neurocognitive Function: A Systematic Review. Clin J Pain. 2018 Mar;34(3):262-275. DOI: 10.1097/AJP.0000000000000536. PMID: 28719507.
8. Pransky GS, Fassier JB, Besen E, Blanck P, Ekberg K, Feuerstein M, et al.; Hopkinton Conference Working Group on Workplace Disability Prevention. Sustaining Work Participation Across the Life Course. J Occup Rehabil. 2016 Dec;26(4):465-479. DOI: 10.1007/s10926-016-9670-1. PMID: 27704342.
9. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016 Dec;46(3):319-29. DOI: 10.1016/j.semarthrit.2016.08.012. PMID: 27916278.
10. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham III CO, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative.Arthritis & rheumatism. 2010 Sep; 62(9):2569-81. DOI: https://doi.org/10.1002/art.27584.
11. Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 1991 May;34(5):505-14. DOI:10.1002/art.1780340502. PMID: 2025304.
12. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 1986 Aug; 29(8):1039-49. DOI: 10.1002/art.1780290816. PMID: 3741515.
13. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. Arthritis Rheum. 1990 Nov; 33:1601-10. DOI: 10.1002/art.1780331101. PMID: 2242058.
14. Isik A, Koca SS, Ozturk A, Mermi O. Anxiety and depression in patients with rheumatoid arthritis. Clin Rheumatol. 2007 Jun; 26(6):872-8. DOI: 10.1007/s10067-006-0407-y. PMID: 16941197.
15. Lok EY, Mok CC, Cheng CW, Cheung EF. Prevalence and determinants of psychiatric disorders in patients with rheumatoid arthritis. Psychosomatics. 2010 Jul-Aug;51(4):338-338.e8. DOI: 10.1176/appi.psy.51.4.338. PMID: 20587762.
16. VanDyke MM, Parker JC, Smarr KL, Hewett JE, Johnson GE, Slaughter JR, et al. Anxiety in rheumatoid arthritis. Arthritis Rheum. 2004 Jun 15;51(3):408-12. DOI: 10.1002/art.20474. PMID: 15188326.
17. Esen SA, Karabulut Y, Esen I, Atmis V. Effects of the Disease Characteristics and the Treatment on Psychological Status in Patients with Rheumatoid Arthritis and Ankylosing Spondylitis. Current Rheumatology Reviews. 2018 Nov 1;14(3):271-278. DOI: 10.2174/1573397113666170728123518. PMID: 28758586.
18. Senra H, Rogers H, Leibach G, Altamar MLP, Plaza SLO, Perrin P, et al. Health-related quality of life and depression in a sample of Latin American adults with rheumatoid arthritis. Int J Rheum Dis. 2017 Nov;20(11):1684-1693. DOI: 10.1111/1756-185X.12412. PMID: 25291016.
19. Ozcetin A, Ataoglu S, Kocer E, Yazici S, Yildiz O, Ataoglul A, et al. Effects of depression and anxiety on quality of life of patients with rheumatoid arthritis, knee osteoarthritis and fibromyalgia syndrome. West Indian Med J. 2007 Mar;56(2):122-9. DOI: 10.1590/s0043-31442007000200004. PMID: 17910141.
20. Meade T, Manolios N, Cumming SR, Conaghan PG, Katz P. Cognitive Impairment in Rheumatoid Arthritis: A Systematic Review. Arthritis Care Res (Hoboken). 2018 Jan;70(1):39-52. DOI: 10.1002/acr.23243. PMID: 28371512.

21. Bell T, Trost Z, Buelow MT, Clay O, Younger J, Moore D, Crowe M. Meta-analysis of cognitive performance in fibromyalgia. J Clin Exp Neuropsychol. 2018 Sep;40(7):698-714. DOI: 10.1080/13803395.2017.1422699. PMID: 29388512.
22. Wu YL, Huang CJ, Fang SC, Ko LH, Tsai PS. Cognitive Impairment in Fibromyalgia: A Meta-Analysis of Case-Control Studies. Psychosom Med. 2018 Jun;80(5):432-438. DOI: 10.1097/PSY.0000000000000575. PMID: 29528888.
23. Zhang Y, Liang D, Jiang R, Ji X, Wang Y, Zhu J, et al. Clinical, psychological features and quality of life of fibromyalgia patients: a cross-sectional study of Chinese sample. Clin Rheumatol. 2018 Feb;37(2):527-37. DOI: 10.1007/s10067-017-3872-6. PMID: 29027043.
24. Katz RS, Heard AR, Mills M, Leavitt F. The prevalence and clinical impact of reported cognitive difficulties (fibrofog) in patients with rheumatic disease with and without fibromyalgia. JCR: Journal of Clinical Rheumatology. 2004 Apr;10(2):53-8. DOI: 10.1097/01.rhu.0000120895.20623.9f. PMID: 17043464.
25. Tomašević-Todorović S, Bošković K, Filipović D, Naumović N. Assessment of memory in patients with rheumatoid arthritis. Vojnosanit Pregl. 2011 Jun;68(6):481-8. DOI: 10.2298/vsp1106481t. PMID: 21818914.
26. Roldán-Tapia L, Cánovas-López R, Cimadevilla J, Valverde M. Cognition and perception deficits in fibromyalgia and rheumatoid arthritis. Reumatología Clínica (English Edition). 2007 May;3(3):101-9. DOI: 10.1016/S1699-258X(07)73676-8. PMID: 21794411.
27. Innes KE, Sambamoorthi U. The Association of Perceived Memory Loss with Osteoarthritis and Related Joint Pain in a Large Appalachian Population. Pain Med. 2018 Jul 1;19(7):1340-1356. DOI: 10.1093/pm/pnx107. PMID: 28525629.
28. Jurišić-Škevin A, Grbović V, Stanković I, Radunović A, Nurković J, Milošević B, et al. The impact of pain on functionality and health related quality of life in patients with knee osteoarthritis. Srpski arhiv za celokupno lekarstvo. 2019;147(1-2):45-51. DOI: https://doi.org/10.2298/SARH171020009J
29. Häuser W, Fitzcharles MA. Facts and myths pertaining to fibromyalgia. Dialogues Clin Neurosci. 2018 Mar;20(1):53-62. DOI: 10.31887/DCNS.2018.20.1/whauser. PMID: 29946212.
30. Nerurkar L, Siebert S, McInnes IB, Cavanagh J. Rheumatoid arthritis and depression: an inflammatory perspective. Lancet Psychiatry. 2019 Feb;6(2):164-73. DOI: 10.1016/S2215-0366(18)30255-4. PMID: 30366684.
31. Bonilla-Jaime H, Sánchez-Salcedo JA, Estevez-Cabrera MM, Molina-Jiménez T, Cortes-Altamirano JL, Alfaro-Rodríguez A. Depression and Pain: Use of Antidepressants. Curr Neuropharmacol. 2022;20(2):384-402. DOI: 10.2174/1570159X19666210609161447. PMID: 34151765; PMCID: PMC9413796.
32. Tang B, Meng W, Hägg S, Burgess S, Jiang X. Reciprocal interaction between depression and pain: results from a comprehensive bidirectional Mendelian randomization study and functional annotation analysis. Pain. 2022 Jan 1; 163(1):e40-e48. DOI: 10.1097/j.pain.0000000000002305. PMID: 34924553; PMCID: PMC8675051.

Table 1. Demographic characteristics and pain among groups

Characteristics		**CO**	**RA Medium DA**	**RA High DA**	**OA**	**FM**
N		30	26	14	40	30
Sex (n, %)	**M**	3 (10)	7 (26.92)	4 (28.57)	14 (35)	3 (10)
	F	27 (90)	19 (73.08)	10 (71.42)	26 (65)	27 (90)
Years (X ± SD)		48.3 ± 6.42	47.81 ± 7.53	48.47 ± 5.90	59 ± 10.31	55.1 ± 12.71
Pain (X ± SD)		Without pain	53.19 ± 22.01	58.54 ± 19.25	52.10 ± 18.79	*66.07 ±22.05

X – mean value; SD – standard deviation; CO – control group; RA – rheumatoid arthritis; DA – disease activity; OA – osteoarthritis; FM – fibromyalgia;

*statistically significant ($p < 0.05$)

Table 2. Results of psychological tests in patients with chronic pain compared to the control group

Parameter	CO	RA-MDA	RA-HDA	OA	FM
BDI (X ± SD)	6.93 ± 4.49	16.39 ± 12.65*	19.13 ± 10.25*	12.72 ± 8.4	18.18 ±12.61*
STAI-S (X ± SD)	41.63 ± 7.83	52.25 ± 5.66	55.17 ± 5.01*	53.12 ± 6.94	54.68 ± 6.34
STAI-T(X ± SD)	40.73 ± 8.01	49.06 ± 6.86	50.04 ± 6.84	49.15 ± 6.24	49.32 ± 6.57
WMS (X ± SD)	136.37 ± 6.07	125.11 ± 14.18*	124.08 ± 13.03*	108.95 ± 19.05**	123.75 ± 15.39*

X – mean value; SD – standard deviation; CO – control group; DA – disease activity; RA – rheumatoid arthritis; MDA – medium disease activity; HDA – high disease activity; OA – osteoarthritis; FM – fibromyalgia; BDI – Beck's Depression Inventory; STAI-S – Spielberger Trait Anxiety Inventory State; STAI-T – Spielberger Trait Anxiety Inventory Traité; WMS – Wechsler Memory Scale;

*statistically significant ($p < 0.05$);

**highly statistically significant ($p < 0.001$)

