The association between anxiety and depression symptoms and clinical and pain characteristics in patients with hip and knee osteoarthritis

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Abstract

Objectives. This study aimed to estimate the prevalence of anxiety and depression symptoms and explore the association between these symptoms and clinical and pain characteristics in patients with chronic pain (CP) due to hip and knee osteoarthritis (OA).

Methods. In this cross-sectional study, adult patients with CP and knee and/or hip OA were included. Anxiety and depression symptoms were assessed using the Hospital Anxiety and Depression Scale. Visual analogue scale, Western Ontario and McMaster Universities Arthritis Index (WOMAC) and PainDetect Questionnaire assessed pain characteristics and Health Assessment Questionnaire (HAQ) evaluated functional disability. Correlation coefficients were used to explore the associations between anxiety and depression symptoms and clinical and pain characteristics.

Results. A total of 61 patients (age 66.2±9.4 years, 67.2% female) were included. Most patients (70.5%) had clinically significant anxiety and/or depression symptoms. Patients with anxiety and/or depression symptoms had higher pain severity (p=0.032) and disability (p=0.014). Depression symptoms had a moderate positive correlation with WOMAC physical function subscale (r=0.520), WOMAC total (r=0.511) and HAQ (r=0.405).

Conclusions. Anxiety and depression symptoms are prevalent in knee or hip OA patients with CP and were associated with higher pain severity and functional disability. These findings support the screening of anxiety and depression symptoms in OA patients, in order to develop more effective multidisciplinary treatments.

Keywords: Osteoarthritis; Affective symptoms; Chronic pain; Pain severity; Disability

Introduction

Osteoarthritis (OA) is one of the most common musculoskeletal diseases worldwide.[1] There seems to have been an increase of around 132% in cases since 1990 and it is expected an increase of approximately 60 to 100% by 2050, depending on the joint affected.[2] The most commonly affected joint worldwide is the knee with an overall prevalence of 22.9% from the age of 40.[3,4] As far as Portugal is concerned, according to EpiReumaPT data, the combined prevalence of hip, knee and hand OA in adults is 19.1% .[5] In fact, nowadays OA is the leading cause of chronic disability in individuals over the age of 70 and has been found to be 11th largest contributor to global disability.[6]

OA is characterized by loss of articular cartilage and subchondral bone sclerosis, resulting in chronic pain (CP), stiffness and functional disability.[3,7] This is a complex disease with multiple components, namely biomechanical, inflammatory and metabolic, encompassing several phenotypes.[6] Therefore, CP in OA has a multifactorial aetiology, associated with various risk factors such as genetics, joint pathology, neurobiological mechanisms and sociocultural or psychological factors.[8]

Previously, OA pain was classified only as nociceptive pain, with peripheral sensitization being mainly associated with tissue damage or inflammation of the joint.[9,10] However, over time it has become clear that persistent nociceptive inputs, originated in a degenerative joint, result in central sensitization.[9,10] Therefore, recent studies have shown that CP in patients with OA has not only a nociceptive but also a neuropathic component, mainly due to the peripheral nerve involvement associated with the joint damage.[11]

In addition, patients with CP have more psychiatric disorders, the most common of which being major depression, with a prevalence of around 49%, and anxiety disorders, with a prevalence of around 33%.[12] In fact, a previous study revealed that the majority of patients with chronic low back pain, have more anxiety and depression symptoms, with a prevalence of 72.9% and 58.1% respectively, with impact on pain severity and disability.[13] Furthermore, patients with chronic neuropathic pain (NP) also reported having more depression and anxiety symptoms, which significantly affected their quality of life.[14,15] Hence, these psychological symptoms also seem to be associated with social and occupational aspects, such as low educational levels and unemployment.[16,17] However, the literature is scarce regarding the prevalence of anxiety and

depression symptoms in patients with CP related to OA and the association of these symptoms with clinical aspects, pain descriptors (including NP descriptors) and functional disability.

Thus, this study aimed to estimate the prevalence of anxiety and depression symptoms and explore the association between these symptoms and clinical and pain characteristics (including NP) in patients with CP due to hip and knee OA.

Materials and Methods

Study Design and Participants

This is a cross-sectional study that was conducted in a Rheumatology department at a tertiary Hospital centre.

Participants included were adult patients with 18 years or older and a diagnosis of OA of the knee and/or hip with CP. The diagnosis of OA was in accordance with the American College of Rheumatology (ACR).[18,19] Both primary and secondary OA cases were included. Secondary cases were due to other inflammatory rheumatic diseases and had to be in remission according to ACR/EULAR criteria, including normal inflammatory parameters. Conventional radiographs bilaterally in load (face and profile) of the knee and hip were taken. Knee OA cases classified as grade 2 to 4 in the Kellgren & Lawrence classification[20] and hip OA cases classified as grade 1 to 3 in the Tönnis classification were included.[21] CP was defined as pain that persists or recurs for more than 3 months, according to the International Association for the Study of Pain.[22] Patients with cancer pain, with psychiatric or cognitive illness that could interfere with data collection, those unable to communicate or speak Portuguese, those with peripheral neuropathy, fibromyalgia, intra-articular corticoid or platelet-rich plasma infiltrations in the last 3 months and surgical procedures on the joint involved were excluded. A total of 64 patients were invited to participate, but only 61 agreed to take part.

All participants were informed about the purpose and details of the study and signed an informed consent after agreeing to take part. The study obtained approval from both the National Committee for Data Protection and the Ethical Committee of the Centro Hospitalar Universitário do São João/Faculdade de Medicina da Universidade do Porto.

Data Collection

In the rheumatology appointment, a trained interviewer performed the recruitment and applied a semi-structured questionnaire in a face-to-face interview. The semi-structured questionnaire included sociodemographic data, such as sex, age, weight, height, academic qualifications, occupation, and medical comorbidities. Medical comorbidities were assessed using the age-adjusted Charlson Comorbidity Index (CCI), which is a weighted index that predicts the probability of death due to comorbidities, taking into account age and a list of 19 medical conditions.[23,24] Effectively, CCI seems to be a highly statistically significant predictor of mortality after adjusting for age, sex, and disease state, namely OA.[25] The Portuguese version of the Hospital Anxiety and Depression Scale (HADS) was used to obtain data on anxiety and depression symptoms.[26]

To characterize OA and associated pain, the following data was collected: onset of pain, date of OA diagnosis, OA location, current medication for pain and anxiety/depression symptoms and supplements (glucosamine and chondroitin sulfate). Pain severity was assessed by the visual analogue scale (VAS).[27,28,29] Pain-related disability was evaluated with the Western Ontario and McMaster Universities Arthritis Index (WOMAC).[30] A Portuguese translation, adaptation, and validation study of the WOMAC has been performed by our research team showing a good performance of this scale; and will be published soon. The Portuguese version of Health Assessment Questionnaire (HAQ)[31,32] was applied to estimate functional disability. To screen and characterize NP, the Portuguese Version of PainDetect questionnaire (PD-Q) was used.[33,34]

Missing information was completed with the patient's clinical records.

Measures

HADS is a self-administered questionnaire subdivided into two subscales, namely depression (HADS-D) and anxiety (HADS-A), which are assessed separately. Each subscale contains seven questions that are measured in a 4-point Likert scale (0-3), so that the scores for each subscale range from 0 to 21. After the individual sum for each subscale, anxiety/depression symptoms can be classified as: normal (0-7), mild (8-10), moderate (11-14) and severe (15-21). A score ≥8 on each subscale reflects clinically significant symptoms of anxiety/depression. The Cronbach's

alpha coefficient described for the depression subscale was 0.81 and for the anxiety subscale 0.76, which were considered as adequate.[26]

The VAS consists of a bidirectional 10cm straight line with two descriptors of pain/disease severity at both ends of the line. The patients marked a cross on the line and subsequently the distance between the end with the lowest severity and the cross was measured.[27,28] In this case, the VAS was used in two individual questionnaires for the knee and hip joints. In each, it was used three times to answer the following questions: effect of illness on well-being during the last week, pain in the left knee/hip during the last week and pain in the right knee/hip during the last week. While in the first question the descriptors chosen were “very well” and “very badly”, in the remaining questions the terms “no pain” and “unbearable pain” were used. Current findings indicate that VAS scores may be labelled as “no pain” (<0.5cm), “mild pain” (0.5-4.4cm), “moderate pain” (4.5-7.4cm) and “severe pain” (7.5-10cm).[27] To simplify the data analysis, when patients experienced pain in the same joint on both sides, the pain severity scale score was averaged.

The WOMAC is a self-administered questionnaire for hip and/or knee OA that is divided into three subscales: pain, joint stiffness, and physical function for daily life activities. This scale has a total of 24 questions, five of which related to pain, two to joint stiffness and 17 to physical function. A five-point Likert scale (0-4) is used for each question, representing different degrees of intensity/difficulty: none (0), mild (1), moderate (2), severe (3) and extreme (4). Each subscale scores are calculated separately, with a possible range of 0-20 points for pain, 0-8 points for stiffness and 0-68 points for physical function, making a total aggregate score of 0-96 points. The higher the score, the greater the patient’s limitations in terms of pain, stiffness, and physical function and the worse their health status.[30,35,36] Moreover, this index has previously been shown to be valid and reliable in assessing patients with knee OA.[37]

The HAQ is an instrument with 20 questions on activities of daily living, divided into eight components.[31] For each question, there are four possible answers: no difficulty (0), some difficulty (1), much difficulty (2), and unable to do (3). Each component is assigned the score of the question with the highest score. If the patient uses aids, the highest score must be increased by two levels. In the end, the average of the eight components is calculated, and the final score can vary between 0 and 3. It should be noted that the scale is not truly continuous, and there are 25 possible values (i.e., 0, 0.125, 0.250…).[31,38] The final score is interpreted as follows: mild to moderate difficulty (0-1), moderate to severe disability (1-2) and severe to very severe

disability (2-3).[39] This questionnaire can be administered in an interview and has been used before in samples of OA patients.[40]

PD-Q is a self-administered questionnaire divided into four parts. The first part includes three items answered on a 11-point Likert scale to assess pain at the moment and over the last four weeks. The second part is a multiple-choice question with 4 graphs representing the pattern of pain intensity over time. In the third part, the patient is asked to identify the areas of pain and irradiation on a sensory map with a human figure. The fourth part includes 7 questions on a 6-point Likert scale about the abnormal/painful sensations related to NP. The total score is obtained by adding up the scores from the last three parts and can range from -1 to 38. A score of -1-12 points shows that NP is very unlikely to be present (<15%), 13-18 points is regarded as ambiguous and 19-38 points indicates that NP is very likely to be present (>90%).[33,34] PD-Q has a significant correlation with the central sensitization mechanisms in OA, as determined in previous studies.[41,42]

Statistical Analysis

Descriptive statistics for continuous variables were described with mean, standard deviation, minimum and maximum if there was a normal distribution data and median, quartile 1 and quartile 3 in the case of a non-normal distribution data. Categorical variables were presented using absolute and relative frequencies (percentage). Sociodemographic, CP and clinical characteristics (VAS, WOMAC, HAQ, PD-Q) were described for the total sample and two sub-groups according to HADS - "Anxiety and/or Depression" (AD) sub-group (score of anxiety and/or depression ≥8) and "No Symptoms" (NS) sub-group (score of anxiety and/or depression <8).

To assess the differences between the AD sub-group and the NS sub-group, the independent-samples *t* test was used for the continuous variables with a normal distribution and the Mann-Whitney *U* test for continuous variables without a normal distribution. For categorical variables, the chi-square test was performed, and if more than 20% of the cells had a count of less than 5, Fisher's Exact test was applied.

To explore the associations between anxiety/depression symptoms (HADS-D, HADS-A and HADS-total scores) and clinical and pain characteristics (including NP) and functional disability, Pearson correlation coefficient was used. When one of the variables analysed presented outliers, the Spearmen coefficient was used.

During all the analysis, a type I error probability (α) of 0.05 was used, which is a critical level accepted by the scientific community. Finally, data were analysed using the IBM SPSS Statistics version 27.0 program for Mac (IBM Corporation Software Group, New York, United States of America).

Results

Sociodemographic characteristics of the sample, AD sub-group and NS sub-group

As shown in Table I, a total of 43 patients (70.5%) had clinically significant anxiety and/or depression symptoms and 18 patients (29.5%) had no symptoms The majority of patients (n=37, 60.7%) had clinically significant anxiety symptoms, with or without depression symptoms, experienced as "mild" (n=17, 27.9%), "moderate" (n=12, 19.7%) or "severe" (n=8, 13.1%). A total of 25 (41.0%) patients had clinically significant depression symptoms, with or without anxiety symptoms, experienced as "mild" (n=16, 26.2%), "moderate" (n=8, 13.1%), or "severe" (n=1, 1.6%).

The sociodemographic characteristics of the total sample and sub-groups are presented in Table I. A total of 61 patients, mostly female (n=41, 67.2%), with a mean age of 66.2±9.4 years old were included. A total of 29 (48.3%) patients had primary education and the majority of patients were retired (n=38, 62.3%). The mean body mass index (BMI) value was 27.4±4.2. Beyond that, only one patient had no medical comorbidities and those who did had a median CCI of 2.0 (1.0-6.0). Regarding the two sub-groups, no statistically significant differences were found in relation to all sociodemographic variables.

Clinical and pain characteristics of the total sample and by defined sub-groups

Table II describes the clinical and pain characteristics for the total sample and both sub-groups. The most common type of OA was primary (n=34, 55.7%). Secondary OA (n=27, 44.3%) was associated with other inflammatory rheumatic conditions, namely 14 patients with microcrystalline arthropathy, 6 patients with rheumatoid arthritis, 5 patients with spondylarthritis and 2 patients with psoriatic arthritis. The most common OA location was the knee (n=31, 52.5%).

Regarding the total sample, the median duration of pain was 10 (3.0-20.0) years and the median time since the OA diagnosis was made was 4.0 (2.0-14.0) years. The diagnosis median duration was higher in the AD sub-group [5.0 (2.0-15.0) years] compared to the NS sub-group [3.0 (1.3-9.8) years]. However, this difference was not statistically significant. Considering the total sample, 27.9% of the participants were taking antidepressant medication. Selective serotonin reuptake inhibitors (SSRIs) (n=12, 70.6%) were the most used class. The AD sub-group had patients taking medication in all classes of antidepressants, while the NS sub-group only used SSRIs. The most used type of pain medication for the total sample were oral NSAIDs (n=41, 68.3%) and weak opioids (n=29, 48.3%). Patients in the AD sub-group were more frequently medicated for pain in all pharmacological classes in comparison to the NS sub-group. However, there were no statistically significant differences between the sub-groups regarding antidepressant and analgesic medication.

Regarding VAS well-being and pain scales for both knee and hip joints, the total sample and both sub-groups had median scores indicating moderate scores without statistically significant differences between the sub-groups. Regarding the WOMAC, the AD sub-group had statistically significant higher scores on the pain (p=0.032) and physical function subscales (p=0.014) and on the total score (p=0.013). According to PD-Q, probable NP was observed in 4 (6.6%) patients, being present only in the AD sub-group. NP was ambiguous in 26.2% of the sample and was present in both sub-groups, without a statistically significant difference. Evaluating functional disability using the HAQ, a mean score of 1.5±1.0 for the total sample was observed, indicating moderate to severe disability. The AD sub-group (1.6±0.9) had a higher score than the NS sub-group (1.1±0.9), despite this was not statistically significant.

Association between anxiety and depression symptoms and clinical and pain characteristics

Table III describes correlations between anxiety (HADS-A) and depression (HADS-D) symptoms and clinical and pain characteristics (pain and disease duration, VAS, WOMAC, PD-Q and HAQ). HADS-A had no correlation with the different variables analysed. HADS-D had a moderate positive correlation with the WOMAC physical function score ($r=0.520$; $p<0.001$), WOMAC total score ($r=0.511$; $p<0.001$) and the HAQ score ($r=0.405$; $p=0.001$). HADS-D had a low positive correlation with WOMAC pain score ($r=0.358$; $p=0.005$) and WOMAC stiffness score ($r=0.364$; $p=0.004$). Low positive correlations were observed between HADS-total and WOMAC pain score ($r=0.363$; $p=0.004$), WOMAC physical function score ($r=0.322$; $p=0.012$), WOMAC total score

(r=0.353; p=0.006) and HAQ score (r=0.311; p=0.015). No correlations were observed between HADS-D and pain duration, diagnosis duration, VAS and NP.

Discussion

This study demonstrated that the majority of patients with CP due to knee and/or hip OA had clinically significant anxiety and/or depression symptoms and that the presence of these symptoms was associated with increased pain severity and physical disability scores. Moreover, depression symptoms were correlated with lower functional disability (HAQ score) in these patients.

In this study, patients with knee and/or hip OA had an average age of 66.2 years, ranging from 42 to 82 years, and were mostly female. As other studies have shown, OA is more common in women and cases start to increase from the age of 50, with a peak between the ages of 70 and 79.[3,4] Despite previous studies highlighting an association between anxiety/depression symptoms and sociodemographic characteristics, namely unemployment and lower educational levels, in our study no statistically significant differences were detected in regard to these variables.[16,17] The most common OA location seems to be firstly the knee and secondly the hip[5], which are the two types covered in the same order by our study. In our sample the most used pain drugs were oral NSAIDs (68.3%) and weak opioids (48.3%). This high use of oral NSAIDs seems to be in line with the recommendations of the ACR, which suggests the use of oral NSAIDs as initial treatment for any type of OA location, before any other oral medication.[43] Furthermore, a study, which considered several European countries, also concluded that the most prescribed medications in OA patients were NSAIDS and opioids, with a prevalence of 58.9% and 35.6% respectively.[44] It is worth noting the high use of opioids in OA patients, which is not in accordance with the ACR recommendations, that highlight the modest benefit of opioid therapy when considering their risk of toxicity and dependence.[43] They also warn that less pain relief occurs in the face of long-term treatment of patients with non-cancer CP.[43] Therefore, it would be important to investigate the use of these drugs and consider whether it would be worthwhile to invest in other types of therapies.

In our study, 70.5% of the patients had anxiety and/or depression symptoms, with anxiety symptoms being present in 60.7% of patients and depression symptoms in 41.0%. Previous research showed that the prevalence of anxiety and depression symptoms can be over 50% in patients with CP and that the prevalence of anxiety symptoms is higher than that of depressive

symptoms, as our study revealed.[12,45] The association between CP and depression symptoms is a widely explored topic. Previous literature has shown that there is a complex bidirectional relationship between CP and occurrence and development of depression symptoms .[46,47] However, it is still unclear as to what the starting point is, whether pain generates a state of anxiety/depression or whether it is anxiety/depression that alters the experience of pain. In any case, OA patients need to be screened and monitored for anxiety and depression-related psychiatric disorders to achieve a better control of their well-being and pain. As such, the treatment of OA patients should have a multidisciplinary management, including not only an approach to pain but also a psychosocial assessment, management, and follow-up. In fact, previous literature revealed that it would be important to initiate individualized CP treatment protocols that include an evaluation of the patients' ability and capacity to manage the disease, pain, comorbidities, and associated impairment.[48] Examining the anxiety/depression treatment for the total sample, only 27.9% of patients received medication, primarily SSRIs, despite the overall prevalence of anxiety and/or depression symptoms being 70.5%. This once again reinforces the subtreatment of these symptoms in the clinical practice.

Considering the sub-groups, patients with anxiety and/or depression symptoms seem to be more medicated for pain than the sub-group without these symptoms, probably due to the fact that those patients had higher severity and functional disability scores related to pain. This difference seems more evident for topical NSAIDs (16.7% versus 0%) and weak opioids (54.8% versus 33.3%). In fact, a previous study concluded that one-year treatment with analgesic medication resulted in a greater reduction in knee OA pain severity among patients with depression in comparison with those without depression. These authors suggest that this result could be explained by the fact that the pain in OA is more related to affective symptomatology than to structural joint pathology. [49]

Patients with anxiety and/or depression symptoms experienced higher levels of pain severity and physical disability. This is in line with previous literature, reporting a positive correlation between depressive symptoms and pain severity and physical disability in patients with lower limb OA.[50] Indeed, anxiety/depression symptoms should be considered risk factors for pain and disability in OA patients. Additionally, in our study patients with anxious and depressive symptoms also had worse functionality than patients without these symptoms. There was even an association between depression symptoms and lower functional disability, measured through the HAQ scale. Therefore, in patients with CP due to OA with anxiety and/or depression

symptoms, it is essential to understand how this rheumatic disease and associated comorbidities affect their physical function and daily life activities.

In this study, NP was present in 6.6% of patients with OA. This finding is similar to previous literature, which reported an overall prevalence of 7-10% of NP in the general population.[14] However, a recent systematic review described a higher prevalence (23%) of NP in patients with knee and hip OA.[51] The small sample size of our study may have justified the lower prevalence of NP. Furthermore, in our study, if we also consider ambiguous NP cases, we obtained a NP prevalence of 32.8%. So, it is essential that ambiguous NP should be better explored in the clinical practice, both through a more detailed and targeted physical examination and through other NP assessment tools, in order to avoid underdiagnosis. In our study, probable NP was only present in patients with anxiety/depression symptoms, which is in line with previous research that estimated a prevalence of 30% of depression in patients with NP.[15] This may indicate that a better control and treatment of NP could reduce these symptoms and vice versa. This type of pain does not generally respond to analgesics such NSAIDs or weak opioids, hindering its management.[14] Currently, the first line treatments for NP include gabapentinoids, which seem to be only moderately effective.[14] In our study, only 11.7% of patients were taking gabapentinoids, when probable and ambiguous NP together was present in 32.8% of patients. This suggests that NP may be undertreated in patients with CP due to knee and hip OA.

Thus, there is an important bidirectional association between anxiety/depression symptoms and CP in patients with hip and knee OA. Therefore, in the future, anxiety and depression symptoms should be screened, monitored and treated early on in patients with CP due to OA.

This study had some limitations that need to be addressed. The present study included a small sample, which may have contributed to the absence of statistical significance in certain results. Furthermore, the fact that the study was carried out in the rheumatology department of a tertiary hospital hinders the generalisation of the data to other clinical settings, such as primary healthcare. Another limitation is that the data may not be generalised to other OA locations, such as spine or hands. Patients with secondary OA were also included. Despite having the inflammatory rheumatic disease under control, their inclusion might have led to an increased overestimation of pain, anxiety/depression symptoms, and functional disability. The study also didn't focus on determining the prevalence of specific psychiatric disorders, but rather only on symptoms.

Despite these limitations, the study was conducted in a non-controlled clinical practice setting using real-world data. This study assessed anxiety and depression symptoms in patients with CP due to OA and correlated these symptoms with clinical and pain characteristics. Moreover, it provided a detailed description of pain due to OA and its repercussions on patients' daily life. It should be emphasised that less frequently addressed topics such as NP were covered. Our study allowed us to realize that the treatment and management of OA patients cannot be limited to the joint disease itself and that it must include a biopsychosocial assessment and management due to the close relationship between CP and anxiety/depression symptoms.

In the future, the association between anxiety and depression symptoms and the pain characteristics in patients with OA should be explored in more depth through longitudinal larger-scale studies, that also focus on other clinical settings and other locations of OA.

Conclusion

In this study, the majority of patients with CP due to knee and hip OA had anxiety and/or depression symptoms. Patients with these physiological symptoms had higher pain severity and functional disability scores.

These results underscore the importance of developing distinct and tailored approaches, centred on a multidisciplinary perspective, that emphasise both pain relief and affective symptomatology management.

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Tables and Figures

Table I. Sociodemographic characteristics of the total sample, AD sub-group and NS sub-group.

Sociodemographic and disease characteristics	Total (N = 61)	Anxiety and/or Depression (N = 43, 70.5%)	No Symptoms (N = 18, 29.5%)	*P* Value (Anxiety/Depression vs No Symptoms)
Age, M ± SD; min-max, y	66.2 ± 9.4; 42-82	65.6 ± 9.9; 42-82	67.5 ± 8.1; 48-80	0.480
Female, n (%)	41 (67.2)	31 (72.1)	10 (55.6)	0.210
Education level (N = 60), n (%)				0.464
Primary education	29 (48.3)	22 (52.4)	7 (38.9)	
Basic education	22 (36.7)	13 (30.9)	9 (60.0)	
Secondary education	7 (11.7)	5 (11.9)	2 (11.1)	
Higher education	2 (3.3)	2 (4.8)	0 (0.0)	
Employment, n (%)				0.583
Employed	18 (29.5)	14 (32.6)	4 (22.2)	
Unemployed	5 (8.2)	4 (9.3)	1 (5.6)	
Retired	38 (62.3)	25 (58.1)	13 (72.2)	
BMI, kg/m²				0.205
M ± SD; min-max	27.4 ± 4.2; 19.1-39.2	27.0 ± 4.5; 19.1-39.2	28.5 ± 3.4; 21.9-33.2	
Comorbidity index, (N = 60), Median (Q1-Q3)	2.0 (1.0-6.0)	2.0 (1.0-6.0)	2.0 (1.0-4.0)	0.694

HADS-A, anxiety subscale of Hospital Anxiety and Depression Scale; HADS-D, depression subscale of Hospital Anxiety and Depression Scale; M, mean; SD, standard deviation; y, years; Q1, first quartile; Q3, third quartile; BMI, body mass index.

Table II. Clinical and pain characteristics for total sample and by defined sub-groups.

Clinical Characteristics	Total (N = 61)	Anxiety and/or Depression symptoms (N = 43, 70.5%)	No Symptoms (N = 18, 29.5%)	*P* Value (Anxiety/Depression vs No Symptoms)
Type of OA, n (%)				0.559
Primary	34 (55.7)	25 (58.1)	9 (50.0)	
Secondary	27 (44.3)	18 (41.9.)	9 (50.0)	
Location, n (%)				0.125
Knee	32 (52.5)	19 (44.2)	13 (72.2)	
Hip	9 (14.8)	7 (16.3)	2 (11.1)	
Knee and Hip	20 (32.8)	17 (39.5)	3 (16.7)	
Pain duration, Median (Q1-Q3), y	10.0 (3.0-20.0)	10.0 (3.0-19.5)	11.5 (6.0-20.0)	0.665
Diagnosis duration, Median (Q1-Q3), y	4.0 (2.0-14.0)	5.0 (2.0-15.0)	3.0 (1.3-9.8)	0.243
Antidepressant medication n (%)				
All	17 (27.9)	x	y	
SSRIs	12 (70.6)	7 (58.3)	5 (100.0)	0.245
SNRIs	5 (29.4)	5 (41.7)	0 (0.0)	0.245
TCAs (mirtazapine)	1 (5.9)	1 (8.3)	0 (0.0)	1.000
Pain medication, (N = 60), n (%)				
Paracetamol	10 (16.7)	7 (16.7)	3 (16.7)	1.000
Oral NSAIDs	41 (68.3)	30 (71.4)	11 (61.1)	0.431
Topic NSAIDs	7 (11.7)	7 (16.7)	0 (0.0)	0.091
Weak Opioids	29 (48.3)	23 (54.8)	6 (33.3)	0.128
Strong Opioids	2 (3.3)	2 (4.8)	0 (0.0)	1.000
Gabapentinoids	7 (11.7)	6 (14.3)	1 (5.6)	0.663
Supplements, (N = 60), n (%)	25 (41.7)	20 (47.6)	5 (27.8)	0.153
VAS – Knee (N = 52), Median (Q1-Q3), cm				
Well-being	5.3 (4.0-7.3)	5.5 (3.4-7.6)	5.0 (4.0-6.9)	0.538
Pain	4.8 (1.6-6.8)	4.8 (2.3-7.1)	5.0 (0.1-6.0)	0.487
VAS – Hip (N = 29), Median (Q1-Q3), cm				

Well-being	5.5 (4.2-7.9)	5.7 (3.9-8.4)	5.2 (4.1-6.0)	0.414
Pain	4.8 (2.8-7.9)	4.8 (2.0-8.0)	5.9 (3.6-7.8)	0.634
WOMAC (N = 60), M± SD, Min-Max				
Pain	10.7 ± 4.6; 0-20	11.5 ± 4.3; 4-20	8.7 ± 4.8; 0-16	**0.032**
Stiffness	4.0 ± 2.4; 0-8	4.2 ± 2.3; 0-8	3.3 ± 2.6; 0-8	0.190
Physical function	32.4 ± 15.3; 2-61	35.5 ± 15.0; 8-61	25.1 ± 13.8; 2-51	**0.014**
Total score	47.0 ± 20.6; 2.85	51.3 ± 20.0; 14-85	47.0 ± 20.6;2-71	**0.013**
PD-Q, n (%)				
Unlikely	41 (67.2)	28 (65.1)	13 (72.2)	0.590
Ambiguous	16 (26.2)	11 (25.6)	5 (27.8)	1.000
Probable	4 (6.6)	4 (9.3)	0 (0.0)	0.310
Total score, M ± SD, Min-Max	9.2 ± 6.3; -1-28	9.9 ± 6.4; -1-28	7.5 ± 5.8; -1-17	0.172
HAQ (N = 60), M ± SD, Min-Max				
Total Score	1.5 ± 1; 0-3.0	1.6 ± 0.9; 0.1-3.0	1.1 ± 0.9; 0-2.8	0.077

M, mean; SD, standard deviation; Q1, first quartile; Q3, third quartile ; SSRIs, selective serotonin reuptake inhibitors; SNRIs, serotonin and norepinephrine reuptake inhibitor; TCAs, tricyclic antidepressants; NSAIDs, nonsteroidal anti-inflammatory drugs; VAS, visual analogue scale (< 0.5 cm = no pain; 0.5 – 4.4 cm = mild pain; 4.5 – 7.4 cm = moderate pain; 7.5 – 10.0 cm = severe pain); WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index (the higher the score, the greater the patients limitations in terms of pain, stiffness and physical function); PD-Q, PainDetect Questionnaire (-1 – 12 = very unlikely; 13 – 18 = ambiguous; 19 – 38 = very likely); HAQ, Health Assessment Questionnaire (0 = no difficulty to 3 = unable to do). Weak opioids including tramadol and codeine; strong opioids including oxycodone, tapentadol, fentanyl, buprenorphine and morfine; gabapentinoids including gabapentin and pregabalin and supplements including glucosamine and chondroitin sulfate.

Table III. Correlation coefficients (Pearson and Spearmen) between anxiety and depression symptoms (according to HADS score) and pain duration (years), OA diagnosis duration (years), VAS, WOMAC, PD-Q and HAQ scores.

HADS	Pain years	Diagnosis years	VAS knee (well-being)	VAS knee (pain)	VAS hip (well-being)	VAS hip (pain)	WOMAC Pain	WOMAC Stiffness	WOMAC Physical function	WOMAC Total	PD-Q	HAQ
HADS-A	0.186 (p = 0.192)	0.268 (p = 0.082)	-0.039 (p = 0.782)	0.023 (p = 0.870)	0.287 (p = 0.131)	0.216 (p = 0.261)	0.244 (p = 0.060)	0.093 (p = 0.481)	0.035 (p = 0.791)	0.091 (p = 0.489)	0.232 (p = 0.072)	0.127 (p = 0.333)
HADS-D	-0.235 (p = 0.097)	-0.043 (p = 0.784)	0.239 (p = 0.088)	0.116 (p = 0.415)	0.350 (p = 0.063)	0.204 (p = 0.288)	**0.358 (p = 0.005)**	**0.364 (p = 0.004)**	**0.520 (p < 0.001)**	**0.511 (p < 0.001)**	0.074 (p = 0.572)	**0.405 (p = 0.001)**
Total	-0.008 (p = 0.957)	0.153 (p = 0.327)	0.106 (p = 0.455)	0.079 (p = 0.579)	0,331 (p = 0,079)	0.291 (p = 0.126)	**0.363 (p = 0.004)**	**0.269 (p = 0.037)**	**0.322 (p = 0.012)**	**0.353 (p = 0.006)**	0.194 (p = 0.134)	**0.311 (p = 0.015)**

p value, the statistical significance of the correlation coefficient; HADS, Hospital Anxiety and Depression Scale; HADS-A, anxiety subscale; HADS-D, depression subscale; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; PD-Q, PainDetect Questionnaire; HAQ, Health Assessment Questionnaire.

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