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Prevalence of Neuropathic Pain in Patients with Osteoarthritis

Prevalência de dor neuropática em pacientes com osteoartrite

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Abstract

Objective The aim of this study was to determine the prevalence of neuropathic pain and characterize the quality of life of patients with osteoarthritis who consulted a pain clinic in Southwestern Colombia.

Methods A cross-sectional study was conducted via telephone survey. Participants ≥18 years of age with a diagnosis of osteoarthritis were included. The LANSS questionnaire was used to evaluate symptoms and signs of neuropathic pain, and the Short Form-8 was used to evaluate quality of life.

Results Response rate was 54.1% (46/85). The male-to-female ratio was 5:1, with an average age of 72 ± 10 years. Most participants (91.3%) had severe pain. The prevalence of neuropathic pain was 28.3% (95%CI = 15.99-43.46), and the prevalence of neuropathic pain amongst women was 84.6% (95%CI = 54.55-98.01). Dysesthesias and paroxysmal pain were present in 92.3% of individuals with neuropathic pain. Regarding quality of life, limitations in physical activity were the most significant, as 63% of individuals reported such limitations.

Conclusion Neuropathic pain was found to be prevalent and had a negative impact on physical function, highlighting the need for therapeutic strategies targeted to specific neuropathic pain pathways in patients with osteoarthritis.

Keywords
- chronic pain
- neuralgia
- quality of life
- osteoarthritis

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Resumo

Objetivo O objetivo deste estudo foi determinar a prevalência de dor neuropática e caracterizar a qualidade de vida de pacientes com osteoartrite que consultaram um ambulatório de dor no sudoeste da Colômbia.

Métodos Este foi um estudo transversal realizado por meio de entrevista telefônica. Foram incluídos participantes $\geq$18 anos de idade com diagnóstico de osteoartrite. O questionário *Leeds Assessment of Neuropathic Symptoms and Signs* (LANSS) foi utilizado para avaliação dos sintomas e sinais de dor neuropática e o *Short Form-8* analisou a qualidade de vida.

Resultados A taxa de resposta foi de 54,1% (46/85). A razão homem:mulher foi de 5:1, com média de idade de 72 ± 10 anos. A maioria dos participantes (91,3%) apresentava dor intensa. A prevalência de dor neuropática foi de 28,3% (intervalo de confiança [IC] de 95% = 15,99-43,46) e a prevalência de dor neuropática entre mulheres foi de 84,6% (IC 95% = 54,55-98,01). Disestesias e dor paroxística foram relatadas por 92,3% dos indivíduos com dor neuropática. Em relação à qualidade de vida, as limitações na prática de atividade física foram as mais significativas e relatadas por 63% dos indivíduos.

Conclusão A dor neuropática foi prevalente e tinha impacto negativo na função física. Isso destaca a necessidade de estratégias terapêuticas direcionadas a vias específicas da dor neuropática em pacientes com osteoartrite.

Palavras-chave

- dor crônica
- neuralgia
- qualidade de vida
- osteoartrite

Introduction

Osteoarthritis (OA) is the most common form of arthritis as it affects 3.3% to 3.6% of the global population.[1] Among older adults, OA is one of the leading causes of deaths and disability worldwide, generating high medical expenses in the middle-aged and elderly populations.[2] It is estimated that in the United States, Canada, UK, France and Australia, OA costs account for between 1% and 2.5% of the gross domestic product.[3] OA common symptoms are joint pain, stiffness and swelling. Histological features include inflammation, cartilage damage and osteophyte formation resulting from repair attempts.[4] Approximately 80% of people over the age of 65 have radiographic evidence of OA, with the hip and knee joints being the most affected.[5]

From many years ago the link between joint disease and peripheral neuropathy has been well established.[6] Although historically, the pain associated with OA had been considered exclusively nociceptive, more recently, there is increasing evidence supporting the idea that has a neuropathic component that can co-exist.[7,8] The International Association for the Study of Pain (IASP) states that neuropathic pain (NP) definition must include a central or peripheral lesion of the somatosensory system.[9] The exact mechanism of OA-related peripheral neuropathy remains largely unknown.[10]

The prevalence of NP in the general population is estimated to be between 6.9% and 10%.[11] In individuals with knee or hip OA, NP prevalence is around 23%.[8] NP has significant implications for quality of life (QOL), including sleep disturbances, anxiety, and depression.[12] Given the significant morbidity and mortality of OA there is a need for research addressing the relationship between NP and OA.

Therefore, combined with the paucity of evidence about OA in low- and middle-income countries, the primary aim of this study was to determine the prevalence of NP in patients with OA who consulted the pain clinic in a referral center in Southwestern Colombia. A secondary aim was to explore the QOL of these patients.

Methods

Study Design

A cross-sectional study was conducted through a telephone interview. The survey used the Spanish versions of the Leeds questionnaire for the Evaluation of Symptoms and Signs of Neuropathic Pain (LANSS)[13,14] and the Short Form-8 questionnaire to assess the QOL (SF-8)™.[15] The study was approved by the ethics committees of the Universidad del Valle and the Hospital Universitario del Valle E.S.E (code 016-017).

Setting

Study participants were recruited from the outpatient pain clinic of the University Hospital of Valle (HUV), a tertiary care center in Southwestern Colombia. It has approximately 500 beds and serves as the main referral center covering a network of around 22195 km^2.

Study Population

The study population was identified by searching the registry of patients who consulted the pain clinic in the Department of Physical Medicine and Rehabilitation at HUV. Electronic medical records were reviewed and patients were retrospectively screened for OA according to the International Classification of Disease v.10 (ICD-10) classification

with codes M15 to M19.[16] Participants ≥18 years of age and with a positive diagnosis of primary or secondary OA were included.

Individuals were contacted between March and April 2018. Verbal informed consent was obtained from all participants prior to the interview. Individuals with altered mental or cognitive status, hearing impairment, previous diagnosis of NP of other causes, fibromyalgia, treatment for more than eight weeks with antineuralgic drugs at therapeutic doses,[17] active cancer and autoimmune diseases were excluded.

Variables

Sociodemographic and clinical characteristics, including age, sex, highest academic degree, employment status and location of the worst pain, were collected. Pain characteristics and QOL were collected using the LANSS and the SF-8.[15]

The LANSS consists of two sections. The first section has four questions that explore essential symptoms of NP grouped into dysesthesias (pins and needles, punches), autonomic changes (if the skin looks mottled or red), pain provoked (if the skin is abnormally sensitive to the touch) and paroxysmal pain (if it has electric shocks, jumping or shocking). The second section performs a physical self-evaluation to look for the presence of positive signs of NP, allodynia, and a negative sign, hypoesthesia. A score greater than or equal to 12 is indicative of NP.[14]

The SF-8[15] questionnaire is an abbreviated version of the SF-36 consisting of 8 sub-scales. It evaluates the physical and mental aspects of QOL by asking participants to report the impact that a medical condition has had on various aspect of their life over the past four weeks, and it has been validated in Spanish.[15]

Data Collection

Telephone interviews were carried out over a period of five weeks. Before starting and to avoid cold calling, patients were asked about their health status and the date of their last and next appointment which is a regular activity in the clinic. Two of the principal investigators trained in applying the survey made the phone calls. Responses were recorded on printed questionnaires, and the information was subsequently entered into an Excel database for analysis.

If a patient could not carry out the physical exam or answer the questionnaire independently, such as in the case of older patients having difficulty understanding the questions, a family member was allowed to assist the participant.

Data Analysis

Data analysis was performed using Stata 16 (Stata Corp., TX, US)®. Initially an exploratory analysis of the data was carried out. This was done in order to identify missing data, typing errors, and inconsistent values and then corrected using the medical record or the paper registries.

Univariate descriptive analysis was performed in which measures of central tendency (mean, median) and dispersion (standard deviation, percentiles, maximum and minimum values) were calculated for continuous variables. Categorical variables were described as relative frequencies and percentages. For bivariate analysis, two groups were compared: patients with NP and without NP, using sociodemographic and clinical variables. Two-tail hypothesis tests were conducted based on the type of variable under comparisons; for categorical variables, chi2 or the Fisher's exact test was used and for continuous variables, t-test or the Wilcoxon test was used, as appropriate. Normality was assessed using the Shapiro-Wilk test and equality of variances was assessed using the variance ratio test. Significance was set at a p-value <0.05.

Results

A total of 126 patients with a positive diagnosis of OA were screened from the registry. Of these, 41 were excluded. Eighty-five patients were listed to be interviewed by telephone; the investigators made an average of five call attempts to each of the participants. Thirty-nine patients were discarded: 32 because the telephone number was invalid, inactive, or there was no response; five had died; and two did not consent to participate. Thus, a total of 46 patients with a positive diagnosis of OA were surveyed (54.12% response rate) (►**Fig.1**).

Sociodemographic and clinical characteristics of the participants are summarized in ►**Table 1**. Most participants were female (82.6%), and the mean age was 72 ± 10 years. There were no significant differences in age by sex ($p = 0.35$) or the presence of NP ($p = 0.71$).

Regarding the intensity of pain measured with the Visual Analogue Scale (VAS), 91.3% ($n = 42/46$) had severe pain, corresponding to a score between 7 and 10. In patients with a LANSS score of ≥12, 46.1% rated the intensity of the pain as a 10. Patients perceived the worst pain in the hips (38.5%) and the knee (30.8%) (►**Fig. 2**).

Overall, the prevalence of NP was 28.3% ($n = 13$, 95% CI = 16-43.5). Among women, the prevalence was 84.6% ($n = 11$, 95%CI = 54.5-98). In the segregated analysis of the variables from the LANSS questionnaire, paroxysmal pain was the most prevalent symptom (►**Table 2**). In participants with NP, the two most frequent types of pain were dysesthesia and paroxysmal pain (►**Fig. 3**).

Regarding the assessment of QOL (►**Table 3**), Physical Health was mostly affected by General Health, Role Physical and Bodily Pain sub-scales. 60.9% of participants perceived their General Health to be "fair,", 63% reported "quite a lot" or "complete" limitations in Role Physical and more than half (60.8%) of the participants reported "severe" or "very severe" in Bodily Pain sub-scales. Mental Health was affected by Social Functioning and Mental Health sub-scales and somehow preserved in Role Emotional sub-scale where most participants reported "not at all" or "slight" emotional problems (52.1%).

Discussion

In our study the overall NP prevalence was 28.3%, which can be contrasted with another study that found NP prevalence

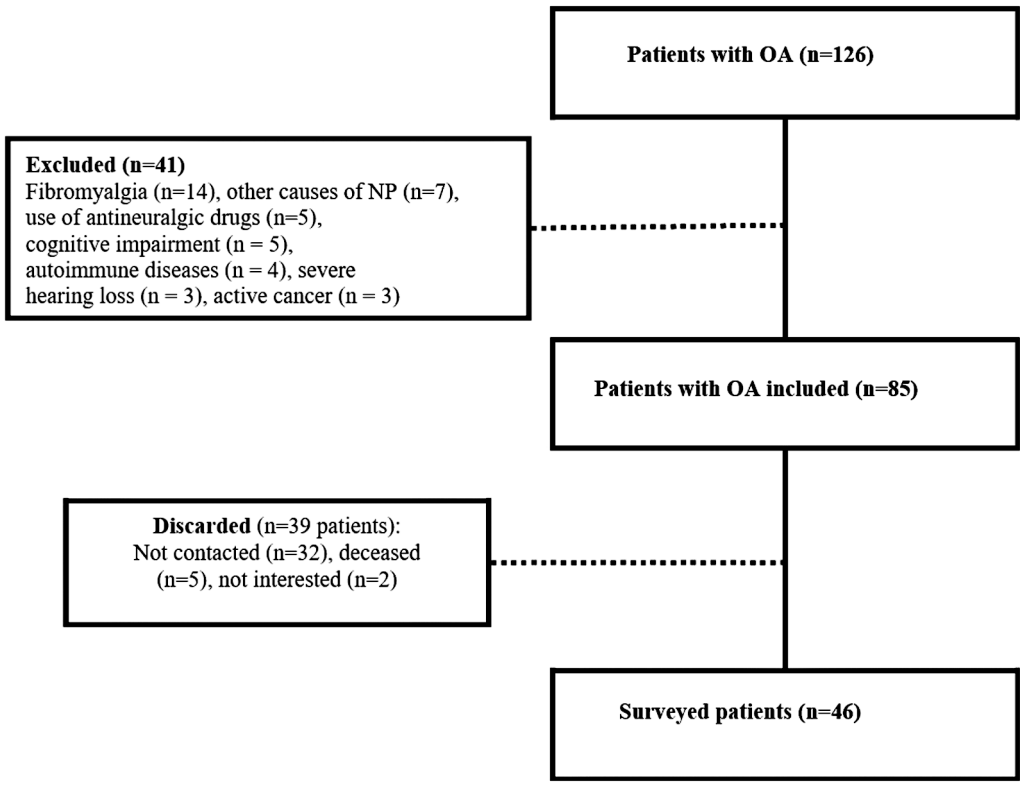

Fig. 1 Patient selection diagram

of 37%; however that study investigated individuals with knee pain exclusively.[18] A systematic review estimated the prevalence of NP amongst individuals with OA to be 23%; however, the review included knee or hip OA.[8] There is a lack of research investigating the presence of NP specifically amongst individuals with OA, and worldwide, there are few studies that characterize the prevalence of NP in those suffering from chronic pain of different etiologies.

Table 1 Sociodemographic and clinical characteristics of the participants

Characteristic	All (n = 46)	Neuropathic Pain		*p* Value
		No (n = 31)	Yes (n = 15)	
Age, mean ± SD	72 ± 10 years	72.68 ± 10.52	71.47 ± 10.24	0.71[+]
Sex: Female, n (%)	38 (82.6)	26 (83.87)	12 (80)	1.0[¶]
Education, n (%)				0.14[¶]
< Primary	25 (54.35)	18 (58.06)	7 (46.67)	
Primary	13 (28.26)	6 (19.35)	7 (46.67)	
> Primary	8 (17.39)	7 (22.58)	1 (6.67)	
Marital status, n (%)				0.92[¶]
Married	19 (41.30)	12 (38.71)	7 (46.67)	
Single/Divorced	17 (36.96)	12 (38.71)	5 (33.33)	
Widowed	10 (21.74)	7 (22.58)	3 (20)	
Employment status: Retired, n (%)	39 (84.78)	27 (87.10)	12 (80)	0.67[¶]
Live in the city: Cali, n (%)	30 (65.22)	21 (67.74)	9 (60)	0.61[‡]
Severe pain: Yes, n (%)	42 (91.3)	27 (87.1)	15 (100)	0.29[¶]
Pain visual analogue scale, median ± IQR	9 (8-10)	9 (8-10)	10 (8-10)	0.36[*]

Abbreviatin: IQR, Interquartile range; LANSS, SD, Standard deviation.
[+]T-test. [¶] Fisher's exact test. [‡] Chi2. [*] Wilcoxon test
►**Table 1** show sociodemographic and presence of neuropathic pain of the participants

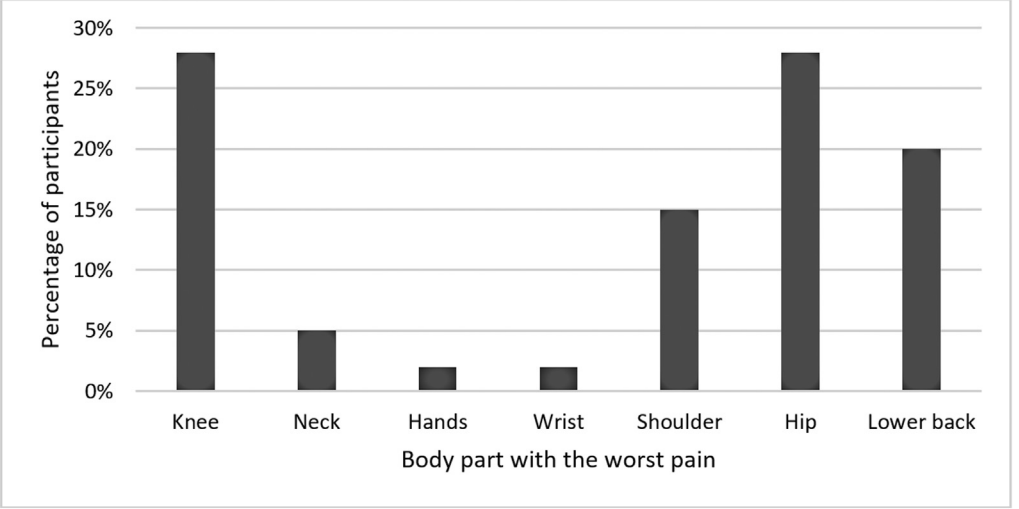

Fig. 2 Perceptions of patients who perceived the worst pain by body area

Table 2. LANSS questionnaire responses

Questionnaire item	Frequency (n = 46)	Percentage (%)
Essential Symptoms		
Dysesthesias	24	52.17
Autonomic changes	6	13.04
Provoked pain	23	50
Paroxysmal pain	27	58.7
Physical Self-evaluation		
Allodynia	14	30.43
Hypoesthesia	19	41.3

►**Table 2** describes LANSS questionnaire items and frequency among participants.

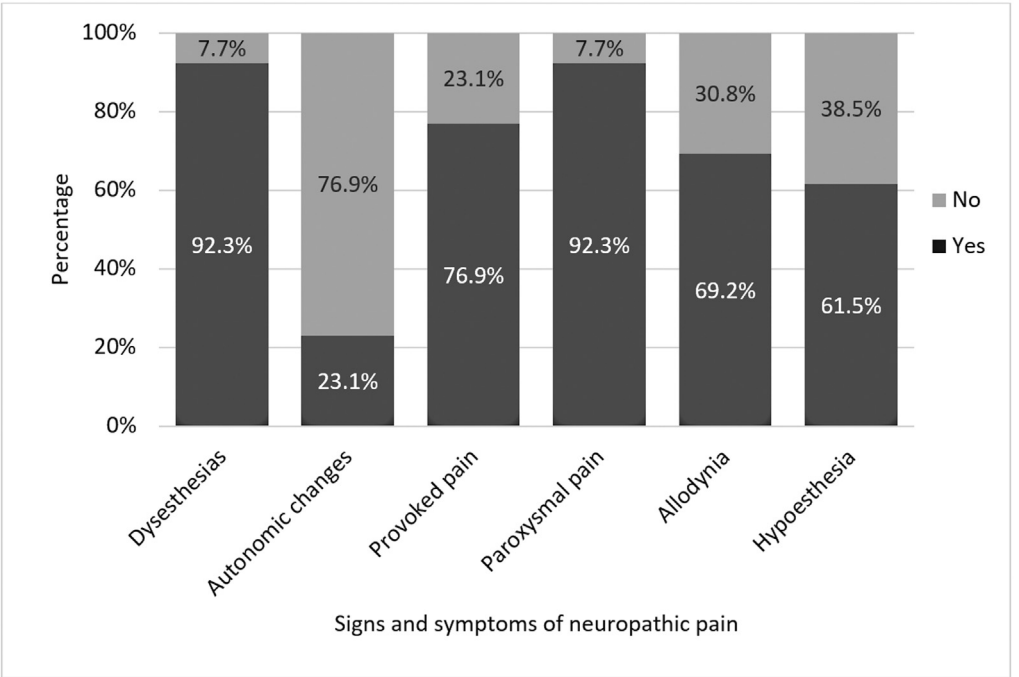

Fig. 3 Frequency of signs and symptoms in patients with neuropathic pain

Table 3 SF-8 Health Survey

Sub-scale	Item	n	%
General health	Excellent	1	2,17
	Very Good	4	8,7
	Good	4	8,7
	Fair	28	60,87
	Poor	5	10,87
	Very Poor	4	8,7
Physical activities limitation (role-physical)	Not at all	3	6,52
	Very little	3	6,52
	Somewhat	11	23,91
	Quite a lot	17	36,96
	Could not do physical activities	12	26,09
Daily work difficulty (physical functioning)	Not at all	9	19,57
	Very little	6	13,04
	Somewhat	9	19,57
	Quite a lot	14	30,43
	Could not do daily work	8	17,39
Bodily pain	None	2	4,35
	Very mild	2	4,35
	Mild	2	4,35
	Moderate	12	26,09
	Severe	19	41,3
	Very severe	9	19,56
Vitality	Very much	3	6,52
	Quite a lot	6	13,04
	Some	16	34,78
	A little	14	30,43
	None	7	15,22
Limitation of usual social activities (social functioning)	Not at all	13	28,26
	Very little	4	8,7
	Somewhat	6	13,04
	Quite a lot	16	34,78
	Could not do social activities	7	15,22
Emotional problems (role-emotional)	Not at all	13	28,26
	Slightly	11	23,91
	Moderately	6	13,04
	Quite a lot	10	21,74
	Extremely	6	13,04
Daily activities limitation because of personal or emotional problems (mental health)	Not at all	5	10,87
	Very little	7	15,22
	Somewhat	14	30,43
	Quite a lot	14	30,43
	Could not do daily activities	6	13,04

Note: ►**Table 3** shows eight sub-scales of the quality-of-life questionnaire with the frequency and percentage on each item evaluated.

Our study found that NP was more prevalent among females, which is in agreement with prior reports.[11,19–21] The reason for this sex difference is not clear. However, it may be related to the hormonal deficiencies that develop in women around menopause, making them susceptible to OA and, therefore, to NP.[19]

Most of the participants (91.3%) reported severe pain. We found that in patients with OA, the hip and knee were reported as areas of the worst pain. NP among those with hip pain was overrepresented, since the prevalence was 38.5%, while the prevalence of NP in other areas of OA pain was 28.3%. Our findings show a high frequency of hip pain, contrasting reports from Latin America, that estimate 31.2% prevalence of knee OA, and only 1.3% of had hip OA.[22] The high rates of hip OA in our study may be because most of the participants were female (82.6%) and past menopause, as it has been found that hormonal changes may be a risk factor for hip OA.[20,21]

In assessment of QOL, social functioning sub-scale half of the participants reported either "quite a lot" or "complete" limitations. As the average age of patients was 72 years old, these limitations in social functioning may be attributed to factors such as the narrowing social networks and changes in social roles that can occur with increasing age.[23] At the same time, most of the participants reported "slight" or "no" emotional problems (52.1%), which could reflect the increased emotional stability that may also come with increasing age.[23] However, 43% reported "quite a lot" or "complete" limitations in their daily activities due to personal or emotional reasons (mental health). As both social and daily physical functioning contribute to healthy aging,[24] there is a need to further investigate the effect that OA and NP on social and emotional factors in the elderly.

As previously mentioned, OA pain can be nociceptive and neuropathic.[10] There have been three important factors identified in the origin of OA pain. First is the increase of cytokines and interleukins in the synovial fluid locally in the joint. Second, general factors such as biomechanical and biochemical alterations due to obesity or diabetes. Third, neuroplastic changes such as peripheral sensitization due to the overgrowth of nerve fibers in articular cartilage that is not typically reversed,[25] this mechanism could be the most significant with regard to the onset of NP in OA, as the NP definition must include a structure of the somatosensory system altered.[8–10]

Currently, in Colombia, the predominant treatment for OA is paracetamol and non-steroidal anti-inflammatory agents.[22] However, as out study emphasize the prevalence of NP in individuals with OA, our results also highlight the need for more targeted interventions to address OA and NP. Pharmacological options such as Duloxetine already approved for knee OA as a chronic pain condition in other guidelines[5] and Lipid lysophosphatidic acid (LPA) receptor blockade[26] proposed as a pharmacological method to inhibit joint nerve damage should be the focus of further studies in OA and NP.[27] Furthermore, non-pharmacological approaches include treatment tailored to the cognitive processes involved in the phenomenology of pain, such as pain-related catastrophizing, which has proven to be effective in the multidisciplinary management of pain.[28]

Limitations

The LANSS questionnaire validated for telephone application has a sensitivity and specificity of 52% and 78%, respectively. These are relatively low values; however, this is the only relevant questionnaire validated in Spanish for telephone use. Further research is required to validate and evaluate the reliability of other similar tools.

Another limitation is the small sample size which provides relevant information about response rate of participants enrolled in this type of research, information that has not been described in Colombia to the best of our knowledge. We attempted to locate participants with multiple phone calls trying to include as many subjects as possible. The power that we reached based on the sample size ($n = 46$), a null proportion of 37%,[19] an alpha of 5%, and the prevalence that we described of 28.3%, was only 21%. As this is the first study describing OA and NP in Colombia and Latin America, the information may be of use of future researchers to use a different data collection method and to calculate a sample size based on our results.

Strengths

To the best of our knowledge, this is the first study in Latin America to assess both OA and NP. There is a lack of research about this topic around the globe. We used a validated tool to assess the outcome variable (NP). Interviews were carried out by resident physicians thus providing a high-quality data collection given the challenges of a survey that includes self-examination.

Conclusion

In our study, we found that the prevalence of NP in patients with OA was close to 30%. It has been increasingly understood that the pain associated with OA is not purely somatic. Recent evidence shows that there are alterations of the somatosensory system in the arthritic joint. Due to the prevalence of NP in individuals in our study, there is a need for further research investigating the physiological mechanisms behind NP in patients with OA. Understanding differences in the mechanisms of pain allows strategies targeted to specific pain pathways and enables healthcare providers to better predict and understand the patient response to treatments. Therefore, there is a need for further interdisciplinary studies that characterizes NP in individuals with OA.

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Conflict of Interests
The authors declare that they have no conflicts of interest.

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References

1 Sen R, Hurley JA. Osteoarthritis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020
2 Lane NE, Shidara K, Wise BL. Osteoarthritis year in review 2016: clinical. Osteoarthritis Cartilage 2017;25(02):209–215
3 Hunter DJ, Schofield D, Callander E. The individual and socioeconomic impact of osteoarthritis. Nat Rev Rheumatol 2014;10(07): 437–441
4 Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis care & research (2010). 2020;72(02):149–162
5 Hochberg MC, Altman RD, April KT, et al; American College of Rheumatology. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken) 2012;64(04):465–474
6 Sakuta M. [One hundred books which built up neurology (37)-Charcot JM "Leçons sur les Localsations das les Maladies du Cerveau et de la Moelle Epinière faites a la Faculté de Médecine de Paris"(1876-1880)]. Brain Nerve 2010;62(01):90–91
7 McDougall JJ, Linton P. Neurophysiology of arthritis pain. Curr Pain Headache Rep 2012;16(06):485–491
8 French HP, Smart KM, Doyle F. Prevalence of neuropathic pain in knee or hip osteoarthritis: A systematic review and meta-analysis. Semin Arthritis Rheum 2017;47(01):1–8
9 Pain IAftSo. IASP Terminology. IASP Press. https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1698#Neuropathicpain. Published 1994. Updated 14/12/17. [Accessed 05/01, 2021] .
10 Thakur M, Dickenson AH, Baron R. Osteoarthritis pain: nociceptive or neuropathic? Nat Rev Rheumatol 2014;10(06):374–380
11 van Hecke O, Austin SK, Khan RA, Smith BH, Torrance N. Neuropathic pain in the general population: a systematic review of epidemiological studies. Pain 2014;155(04):654–662
12 Colloca L, Ludman T, Bouhassira D, et al. Neuropathic pain. Nat Rev Dis Primers 2017;3:17002
13 Weingarten TN, Watson JC, Hooten WM, et al. Validation of the S-LANSS in the community setting. Pain 2007;132(1-2)189–194
14 López-de-Uralde-Villanueva I, Gil-Martínez A, Candelas-Fernández P, de Andrés-Ares J, Beltrán-Alacreu H, La Touche R. Validity and reliability of the Spanish-language version of the self-administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) pain scale. Neurologia (Engl Ed) 2018;33(08):505–514 (Engl Ed)
15 Vallès J, Guilera M, Briones Z, Gomar C, Canet J, Alonso JARISCAT Group. Validity of the Spanish 8-item short-form generic health-related quality-of-life questionnaire in surgical patients: a population-based study. Anesthesiology 2010;112(05):1164–1174
16 Clasificación estadística internacional de enfermedades y problemas relacionados con la salud: décima revisión (CIE-10), volúmenes 1, 2 y 3 en CD-Rom. Rev Esp Salud Pública 2004; 78:647–648
17 Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol 2015;14(02):162–173
18 Hochman JR, Davis AM, Elkayam J, Gagliese L, Hawker GA. Neuropathic pain symptoms on the modified painDETECT correlate with signs of central sensitization in knee osteoarthritis. Osteoarthritis Cartilage 2013;21(09):1236–1242
19 Felson DT. An update on the pathogenesis and epidemiology of osteoarthritis. Radiol Clin North Am 2004;42(01):1–9, v
20 Wluka AE, Cicuttini FM, Spector TD. Menopause, oestrogens and arthritis. Maturitas 2000;35(03):183–199
21 Prieto-Alhambra D, Judge A, Javaid MK, Cooper C, Diez-Perez A, Arden NK. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. Ann Rheum Dis 2014;73(09): 1659–1664
22 Reginato AM, Riera H, Vera M, et al; Pan-American League of Associations for Rheumatology (PANLAR) Osteoarthritis Study Group. Osteoarthritis in Latin America: Study of Demographic and Clinical Characteristics in 3040 Patients. J Clin Rheumatol 2015;21(08):391–397
23 Charles ST, Carstensen LL. Social and emotional aging. Annu Rev Psychol 2010;61:383–409
24 Beard JR, Officer A, de Carvalho IA, et al. The World report on ageing and health: a policy framework for healthy ageing. Lancet 2016;387(10033(:2145–2154
25 Schaible HG. Osteoarthritis pain. Recent advances and controversies. Curr Opin Support Palliat Care 2018;12(02):148–153
26 McDougall JJ, Albacete S, Schuelert N, et al. Lysophosphatidic acid provides a missing link between osteoarthritis and joint neuropathic pain. Osteoarthritis Cartilage 2017;25(06):926–934
27 Dimitroulas T, Duarte RV, Behura A, Kitas GD, Raphael JH. Neuropathic pain in osteoarthritis: a review of pathophysiological mechanisms and implications for treatment. Semin Arthritis Rheum 2014;44(02):145–154
28 Quartana PJ, Campbell CM, Edwards RR. Pain catastrophizing: a critical review. Expert Rev Neurother 2009;9(05):745–758