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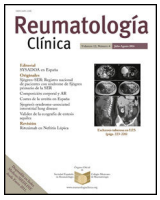

Original Article

The High Clinical Burden of Erosive Hand Osteoarthritis is Associated with Clinical Findings, Pain, and Radiographic Severity

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ABSTRACT

Varying reports exist on the clinical impact of erosive hand osteoarthritis (EHOA) in terms of pain and articular function. Few studies have assessed the association of a patient's clinical features with the presence of more severe radiographic disease. The aim was to evaluate clinical and radiographic characteristics in EHOA comparing with non-erosive (NEHOA); to examine pain and functional impairment between EHOA and NEHOA; and correlate functional impairment with clinical findings, pain, and radiographic severity.

Methods: 62 patients with EHOA and 57 with NEHO were included. Pain was assessed through Visual Analogue Scale (VAS) and Australian/Canadian Osteoarthritis Hand Index (AUSCAN) pain subdomain. Functioning was evaluated with the Health Assessment Questionnaire (HAQ) concerning hand function and AUSCAN. Radiographs were scored with the Kallman scale and subchondral erosions with the Verbruggen–Veys method. Student *t*-tests were used for comparing quantitative data, chi-squared tests for categorical variables, and Pearson or Spearman tests for assessing correlation.

Results: Patients with EHOA reported significantly higher levels of pain on the VAS and AUSCAN ($p < 0.01$). In EHOA, VAS positively correlated with the HAQ and AUSCAN scales (rho = 0.68 and 0.77). In NEHOA, Visual Analogue Scale (VAS) positively and strongly correlated with HAQ and AUSCAN (rho = 0.84 and 0.89). Nodes, Kallman score and erosions showed a positive but weak correlation with HAQ and AUSCAN in both groups.

Conclusion: Both EHOA and NEHOA participants had functional impairment, but the erosive subtype had higher clinical burden and increased joint damage. This higher clinical burden is attributed mainly to pain.

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La elevada carga clínica de la osteoartritis erosiva de mano está asociada con hallazgos clínicos, dolor y severidad radiográfica

Palabras clave:
Osteoartritis de mano
Osteoartritis erosiva y no erosiva de mano
Función

RESUMEN

Existen estudios sobre el impacto clínico de la osteoartritis erosiva de mano (OAEM) en términos de dolor y función articular. Pocos estudios han evaluado la asociación de las características clínicas del paciente con OAEM con la presencia de enfermedad radiográfica más grave. El objetivo fue evaluar las características clínicas y radiográficas en OAEM comparándolas con osteoartritis de mano no erosiva (OANEM), examinar el dolor y deterioro funcional entre OAEM y OANEM y correlacionar el deterioro funcional con los hallazgos clínicos, dolor y severidad radiográfica.

Métodos: Se incluyeron 62 pacientes con OAEM y 52 con OANEM. El dolor se evaluó con Escala Visual Análoga (EVA) y el subdominio de dolor de AUSCAN. La capacidad funcional se evaluó con *Health Assessment Questionaire* (HAQ) relativo a la función de la mano y AUSCAN. Las radiografías se evaluaron con la escala de Kallman y las erosiones subcondrales con el método Verbruggen-Veys. Se utilizó *t* de Student

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para comparar datos cuantitativos, χ^2 para variables categóricas, pruebas de Pearson o Spearman para evaluar la correlación.
Resultados: Los pacientes con OAEM presentaron niveles significativamente más altos de dolor en EVA y el subdominio de dolor de AUSCAN (p < 0,01) y de deterioro funcional por HAQ y Índice de manos de Osteoartritis Australiano/Canadiense (AUSCAN) (p < 0,01). En OAEM, VAS correlacionó positivamente con las escalas HAQ y AUSCAN (rho = 0,68 y 0,77). En OANEM, VAS se correlacionó positiva y fuertemente con HAQ y AUSCAN (rho = 0,84 y 0,89). Los nódulos, puntuación de Kallman y erosiones mostraron una correlación positiva pero débil con HAQ y AUSCAN en ambos grupos.
Conclusión: Los participantes con osteoartritis erosiva y no erosiva de mano presentaron deterioro funcional, pero el subtipo erosivo presentó mayor carga clínica y daño articular. La mayor carga clínica fue atribuida al dolor.

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Introduction

Osteoarthritis (OA) is the most common joint disorder and a leading cause of musculoskeletal disability worldwide. While OA can occur in any joint, the hand is one of the most frequently affected anatomic sites. Indeed, radiographic features of hand OA (HOA) can be found in 67% of women and 55% of men aged 55 years or older.[1] Symptomatic HOA is less common and only prevalent in 26.2% of women and 13.4% of men above 70 years.[2] Instead of mere articular cartilage degeneration, HOA is currently considered an entity affecting the whole joint.

Several risk factors have been associated with developing HOA, with most prominent including female sex, age over 40, menopausal status, family history, obesity, joint laxity, prior injury, and occupational- or recreational-related usage.[3] Clinically, HOA is characterized by pain, joint stiffness, and limitation of movement with a decrease of grip or pinch strength. Patients can show nodes of the affected interphalangeal joints (IPJ) and deformities, such as squaring of the thumb base. Radiographically, HOA is characterized by joint space narrowing, osteophyte formation, subchondral sclerosis, and subchondral cyst formation.[4] HOA is a heterogeneous condition that can be classified into five different subgroups: (1) non-nodal, including distal interphalangeal joints (DIPJ) and proximal interphalangeal joints (PIPJ); (2) nodal, including Heberden and Bouchard nodes (firm swellings over the superolateral and dorsal aspects of the DIPJ and PIPJ, respectively); (3) thumb base or first carpometacarpal joint (1st CMCJ) OA, with or without scaphotrapezial joint (STJ); (4) generalized (meaning HOA plus OA in other sites); and (5) erosive (EHOA), targeting DIPJ and PIPJ, defined radiographically by subchondral central erosions.[5]

EHOA is considered the most aggressive and uncommon subset, prevalent in 5–15% of those with symptomatic HOA and affecting predominantly postmenopausal women with a female:male ratio of 12:1.[6,7] Inflammatory flares with severe pain, joint swelling, and significant functional impairment make up the classical clinical picture. Radiographically, erosive HOA is characterized by the presence of subchondral central bone erosions, cortical destruction, and subsequent reparative changes, which may include bony ankylosis with severe joint destruction, major deformations, and mobility restriction. EHOA carries high consequences in terms of aesthetic discomfort and severe limitation in joint motion, which can severely impair function, in turn affecting working and social activities and, ultimately, patients' quality of life.[5,8–11] This negative impact on general health is comparable to inflammatory—such as rheumatoid—arthritis.[12,13] The presence of erosive lesions on radiographs has been reportedly associated with an increased risk of disability, up to twice as much as in those without radiographic erosions.[8]

Although different reports exist on the clinical impact of EHOA in terms of pain and articular function, few studies have assessed the association between a patient's clinical features with the presence of more severe radiographic disease. Building off of this background, this study aimed to evaluate the clinical and radiographic characteristics of EHOA and non-erosive [NEHOA] in a group of consecutive patients with symptomatic HOA; to examine pain and functional impairment between patients with EHOA and NEHOA; and to correlate functional impairment with clinical findings, presence of pain, and radiographic severity.

Materials and methods

The study protocol was reviewed and approved by the Investigation and Ethics Committee of the *Luis Guillermo Ibarra Ibarra* National Institute for Rehabilitation (INRLGII, for its initials in Spanish) under protocol number 51/15. All participants gave written consent before study initiation. Both male and female patients were recruited from those who sought care at the Rheumatology Outpatient Clinic; inclusion criteria included being aged 40 years or over and having a clinical diagnosis of HOA, according to the American College of Rheumatology (ACR) criteria.[14] The ACR criteria include pain, aching, or stiffness along with hard tissue enlargement involving at least 2 of 10 selected joints and fewer than 3 swollen metacarpal-phalangeal joints, and hard tissue enlargement of at least 2 DIP joints. The ten selected joints refer to the second and third DIPJ, the second and third PIPJ, and the 1st CMCJ of both hands.[14] Patients were excluded if they were identified as having inflammatory arthritis (i.e., rheumatoid arthritis or psoriatic arthritis), and if they did not have complete clinical information or hand radiographs. Demographic and clinical data were collected from each patient, including age, sex, age of disease onset, OA family history, symptoms duration, menopause, hormone therapy, excessive use of hands, damage from trauma, body mass index (BMI, kg/m^2), and comorbidities. A rheumatologist (CDS) physically examined all patients, using pressure palpation to evaluate the interphalangeal joints [DIFJ], proximal interphalangeal joints [PIFJ], and the 1st CMCJ for pain and the presence and count of Heberden's and Bouchard's nodes. Pain was assessed by self-reported pain on a visual analogue scale (VAS) [0 = without pain to 10 = severe pain] and Australian/Canadian Osteoarthritis Hand Index (AUSCAN) pain subdomain.

Hand functional disability

The Stanford Health Assessment Questionnaire (HAQ) concerning hand function and the AUSCAN were used to assess hand functionality.[15–18] The HAQ uses 24 questions to assess eight aspects of disability. To assess hand disability, we utilized the eight questions concerning hand function from the HAQ questionnaire. At the beginning of each item, participants are asked a question starting with "Are you able to?. . ." in reference to the past week. Participants rated the difficulty of the following tasks on a scale from 0 to 3 (0 = no difficulty, 3 = unable to do): The selected

HAQ questions for assessing hand disability were: *1. Dress yourself, including handling of closures? 2. Comb your hair or do your own makeup? 3. Turn taps on and off? 4. Cut your meat and lift a full cup or glass to your mouth? 5. Open a new milk carton? 6. Open car doors? 7. Hold a pen or a pencil? 8. Open jars that have been previously opened?* A score of >0.5 was considered a hand disability, with higher scores indicating greater disability.[15,16] The AUSCAN is a 5-point Likert scale (from 0 = none to 4 = extreme) and possesses 15 items on three dimensions: pain (5 items), stiffness (1 item), and physical function (9 items). A maximum score of 60 points, with subscales for pain (20 points), stiffness (4 points), and physical function (36 points). A greater score signifies more hand disability.[17,18] This questionnaire has been validated in Mexico.[19]

Radiographic assessment

HOA was graded radiographically using the Kallman scale evaluating DIP (5), PIP (4), 1st CMCJ (1), and trapezioscaphoid [TSJ] (1) joints of each hand. Posteroanterior hand radiographs of both hands were performed in all patients and taken at least one month before the clinical examination. On each radiograph, eleven individual joints were graded for the presence and severity of six selected individual features of OA: osteophytes, joint space narrowing, subchondral sclerosis, subchondral cysts, lateral deformity, and cortical collapse. Osteophytes were differentiated into three grades (0 = absent, 1 = small osteophyte, moderate = 2 and large = 3), as well as joint space narrowing (0 = absent, 1 = definitely diminished, 2 = severe, 3 = joint fusion at least at one point), while sclerosis, cysts, lateral deformity, and cortical collapse space were scored as either absent or present (0 or 1 respectively). A lateral deformity was defined as a misalignment of at least 15 degrees. First CMCJ was scored for osteophytes, joint space narrowing, subchondral sclerosis, subchondral cysts, and the TSJ was scored for narrowing joint space, subchondral sclerosis, and subchondral cysts with a total count of 103 points per hand and 206 points for both hands.[20] Erosive HOA was defined by the presence of at least one joint in the erosive or remodelling phase of the subchondral plate, according to the Verbruggen–Veys scoring method.[21] Two trained and experienced observers (CDS and NMA) performed all radiological evaluations, blinded to the patients' clinical data and to each others' readings. Researchers CDS and NMA were standardized on the Kallman scale prior to study commencement, performing blind assessments of 20 pairs of HOA patients' hand X-rays.

Statistical analysis

Data distribution in both groups was assessed through the Shapiro–Wilk test. The mean and standard deviation (SD) or median and interquartile range (IQR) values were reported for continuous variables and frequency and percentage for categorical variables. The comparison of continuous variables was performed using a Student *t*-test for normally distributed data or Mann–Whitney *U* test for non-parametrically distributed data. For categorical variables, a chi-squared (χ^2) statistics test was applied. A Pearson or Spearman test was used to assess the correlation between hand functional disability (HAQ and AUSCAN) with pain (VAS), nodes, Kallman score, or subchondral erosions. The inter-reader-reliability to classified EHOA or NEHOA through Kallman score was analyzed with the Cohen's kappa coefficient (κ). Alpha level was set at 0.05. Version 15.0 of the STATA statistical software package was utilized for calculations.

Results

Our study population was made up of 119 patients with symptomatic HOA, from which 52.1% were classified as EHOA and 47.9% as NEHOA. Demographic data are depicted in Table 1. The mean age was 65.6 ± 8.3 and 59.9 ± 7.3 years, in erosive and non-erosive HOA, respectively ($p = 0.0002$). There were no significant differences in gender distribution when comparing both HOA subsets ($p = 0.1$); women were more affected (87.1% and 94.7%). Age of onset did not show differences between EHOA and NEHOA ($p = 0.3$); however, there were significant differences in disease duration with a longer duration in EHOA ($p = 0.0001$). There were no significant differences between EHOA or NEHOA group and other clinical variables, such as OA family history, BMI, menopause, hormonal therapy, hand injury/hand overuse, or comorbidities ($p > 0.05$). There were significant differences in the number of nodes in the right and left hands, as well as in the total number of nodes ($p < 0.01$) between erosive and non-erosive subgroup. There were no significant differences between the EHOA and NEHOA subgroups in the number of painful joints by palpation ($p = 0.1$). The Kallman score also showed differences with higher scores in EHOA (p 0.01) (Table 1). There was high agreement between the observers ($\kappa = 0.98$).

Participants with EHOA reported significantly higher levels of pain on the VAS and AUSCAN subdomain pain. Hand functionality of patients measured by HAQ and AUSCAN function showed a statistically significant decrease in hand function in EHOA compared with NEHOA ($p < 0.01$) (Table 2).

In the EHOA group, the VAS was positively associated with the HAQ and AUSCAN scales (rho = 0.68 and 0.77; $p = 0.00001$). In the NEHOA group, the VAS was strongly and positively associated with HAQ and AUSCAN scales (rho = 0.84 and 0.89, respectively; $p = 0.00001$). There was a positive weak correlation between HAQ and AUSCAN scales with nodes and Kallman score in EHOA and NEHOA and, erosions in erosive subgroup with HAQ and AUSCAN with a weak correlation (Table 3).

Discussion

The hand is a commonly affected site in OA, and the great majority of patients suffer substantial limitations in their daily activities because of hand pain. EHOA is considered a clinically uncommon subset of HOA, with a worse clinical course, severe structural changes, and with a significant impairment of quality of life.[2,5,12,22] Our results showed a higher prevalence of EHOA (52.1%) among symptomatic HOA than in the Framingham study in which EHOA prevalence in symptomatic HOA was 10.2%.[8,23] Patients with EHOA have been known to experience severe pain with significant functional limitations. Pattrick et al. demonstrated that patients with EHOA had more pain and difficulty in performing tasks than patients with nodal OA and that healthy controls.[11] In that same vein, other studies have demonstrated that EHOA experienced more severe pain and stiffness than those with NEHOA, or than those with no HOA.[8] Our results align with those studies and confirm that EHOA is a more painful entity than NEHOA.

OA is by far more common in women. Our results also showed that both erosive and non-erosive subtypes HOA are much more common in women, as observed previously.[8,23] In our study population, patients with EHOA started with HOA at a similar age than NEHOA. However, the erosive subtype had a longer disease duration and, even though this study did not investigate whether erosive OA was a subgroup of OA[5] or a continuum of HOA with a greater degree of joint damage[22,24,25]; the longer disease and higher severity HOA evidenced by higher Kallman scores in our patients provide evidence that erosive form probably represents an extreme progression of HOA.

EHOA has a higher clinical burden than non-erosive forms, and the associated disability might be as severe as that associated with inflammatory arthritis, such as rheumatoid arthritis.[12,26] Our results showed that HAQ and AUSCAN—including their

Table 1
Clinical and radiological characteristics.

	EHOA($n=62$)	NEHOA($n=57$)	p
Age (mean ± SD: years)	65.5 ± 8.3	59.9 ± 7.3	0.0002[a]
Age of onset (mean ± SD; years)	54.4 ± 7.8	53.3 ± 6.7	0.3[a]
Disease duration (median, IQR; years)	10 (7–15)	5 (3–10)	0.0001[b]
BMI (mean ± SD; kg/m²)	26.9 ± 3.4	26.2 ± 3.6	0.3[a]
Gender			
Women (*n*, %)	54 (87.1)	54 (94.7)	0.1[c]
Men (*n*, %)	8 (12.9)	3 (5.3)	
Number of nodes			
Right hand (median, IQR)	6 (4–9)	3 (2–5)	0.00001[b]
Left hand (median, IQR)	6 (4–7)	2 (1–3)	0.00001[b]
Total nodes (median, IQR)	12 (7–16)	5 (3–8)	0.00001[b]
Kallman score			
Right hand (median, IQR)	47.5 (39–59)	25 (20–31)	0.00001[b]
Left hand (mean ± SD)	49 (39–58)	27 (19–33)	0.00001[a]
Kallman score total (mean ± SD)	101 ± 26.4	54.4 ± 12.4	0.00001[a]
Erosions			
Right hand (median, IQR)	2 (1–4)		
Left hand (median, IQR)	2 (1–4)		
Total erosions	4 (2–8)		

EHOA: erosive hand osteoarthritis; NEHOA: non-erosive hand osteoarthritis; BMI: body mass index; SD: standard deviation; IQR: interquartile range; a: Student *t* test; b: Mann–Withney *U* test; *c*: chi-square test.

Table 2
Comparison between pain and physical function in erosive and non-erosive hand osteoarthritis.

	EHOA ($n=62$)	NEHO ($n=57$)	*P*
Pain VAS (mean ± SD)	5.8 ± 2.5	3.8 ± 1.9	0.00001[a]
HAQ (median, IQR)	1.05 (0.62–1.4)	0.44 (0.25–0.62)	0.00001[b]
AUSCAN (median, IQR)	26 (16–33)	11 (6–17)	0.00001[b]
Pain subscale (median, IQR)	6 (4–9)	3 (1–5)	0.00001[b]
Stiffness subscale (median, IQR)	1.7 ± 0.9	1.1 ± 0.8	0.001[b]
Physical function subscale (median, IQR)	18 (9–21)	7 (3–10)	0.00001[b]

EHOA: erosive hand osteoarthritis; NEHO: non-erosive hand osteoarthritis; VAS: visual analogue scale; HAQ: Health Assessment Questionnaire; AUSCAN: Australian/Canadian Osteoarthritis Hand Index; a: Student *t* test; b: Mann–Withney *U* test.

subscales—showed significant differences, with higher scores in EHOA. Previously, Bijsterbosch et al. reported that patients with EHOA experience more pain and functional limitations, worse hand mobility, and less satisfaction with hand function and aesthetics than those with NEHOA. Self-reported hand function, measured with the AUSCAN scale, was worse in patients with EHOA.[10] In the present study, patients with EHOA had more nodes, which were a determinant of clinical outcome as those with a high number of nodes had a worse outcome. Nonetheless, when controlling for the number of nodes,[10] only hand mobility and patient satisfaction remained significantly different between the groups. Kwok et al.[8] showed that hand disability measured through HAQ was reported in 2.3% of the radiographic HOA population, but 7.3% of the EHOA population. This evidence, taken together, demonstrates that pain and disability are more common in erosive than in non-erosive HOA.

In the present study, VAS showed a positive correlation with HAQ and AUSCAN scales in EHOA, whereas a very strong positive significant correlation was observed between the VAS and HAQ and AUSCAN scales in NEHOA. Additionally, there was a positive correlation ranging from moderate to weak between HAQ and AUSCAN scales with nodes and Kallman score in both EHOA and NEHOA and weak correlation with erosions in erosive form. Previously, it has been shown that a higher number of nodes is related to more pain and self-reported functional limitations.[10] Likewise, Kallman scores are more severe in EHOA than in NEHOA.[24] More recently, Perrotta et al. observed that the Kallman score correlates significantly with the duration of symptoms, AUSCAN and HAQ.[27]

In this study, EHOA patients had increased self-reported pain on the VAS and the AUSCAN questionnaire. EHOA patients also had a greater number of nodes, higher radiographic involvement,

Table 3
Correlation of HAQ and AUSCAN with VAS, nodes, and radiographic characteristics in EHOA and NEHOA.

	Ehoa ($N=62$)		Nehoa ($N=57$)	
	HAQ	AUSCAN	HAQ	AUSCAN
VAS				
rho	0.68	0.77	0.84	0.89
p	0.00001	0.00001	0.00001	0.00001
Nodes				
rho	0.38	0.32	0.52	0.47
p	0.002	0.009	0.00001	0.0002
Kallman score				
rho	0.33	0.23	0.31	0.37
p	0.007	0.07	0.02	0.005
Erosions				
rho	0.30	0.22		
p	0.02	0.09		

EHOA: erosive hand osteoarthritis; NEHOA: non-erosive hand osteoarthritis; HAQ: Health Assessment Questionnaire; AUSCAN: Australian/Canadian Osteoarthritis Hand Index; VAS: visual analogue scale.

and, therefore, most severe functional limitations than their non-erosive counterparts. This HOA clinical burden information agrees with Bijsterbosch et al., who concluded that patients with EHOA have a greater clinical burden than those with non- erosive disease. This clinical detriment is attributed both to the erosive and nodal disease.[10] Pain was the leading cause of functional disability in our study, and it should be considered one of the most important factors in functional impairment in HOA. In other studies, pain is not the predominant symptom for functional

disability in HOA patients; however, in our study, we believe that pain is probably more likely related to inflammatory HOA activity and not chronicity. Evidence suggests that inflammation plays a key role in the pathogenesis of OA[28,29] however, in most patients, the acute phase makers in blood are at normal values. At present, the only OA variant proposed and classified as inflammatory is that of the hand with radiographic erosions, termed erosive HOA.[30]

Like all studies, this work has certain limitations. The first limitation relates to the sample's smaller size, relative to other similar studies. However, in order to compensate this, we tried to accurately classify the HOA subsets to make more precise comparations. The second limitation is that our study, like all hospital-based studies, may have incurred a selection bias. Indeed, we recognize that, as our institution is a tertiary care centre, it is likely that we receive more severe HOA cases. This would imply that the proportion of EHOA cases in our study could be clinically different from that of the general population.

In conclusion, this study corroborates that HOA, in particular, EHOA, correlates with a higher clinical burden and increased joint damage evidenced by worse functionality by HAQ and AUSCAN, more severe pain, nodes, and severe radiographic involvement. Based on these findings, it is our interpretation that each one of these factors (pain, nodes, and radiographic changes) are associated in different magnitude in individuals with erosive and non-erosive HOA, depending on the stage of the disease: either active (inflammatory flares) or chronic stage (structural abnormalities). Pain is an important determinant that substantially contributes to functional limitations in erosive and non-erosive HOA. Thus, future research studies should focus on establishing the active or chronic phase of HOA to provide individualized drug therapy, rehabilitation, or both.

Compliance with ethical standards

All procedures performed in this study were carried out in accordance with the ethical standards of the Ethics and Investigation Committee of the "Luis Guillermo Ibarra Ibarra" National Rehabilitation Institute and with the 1964 Declaration of Helsinki and its later amendments. Likewise, all participants received full and transparent information about the study and signed informed consent prior to being included.

Conflicts of interest

The authors declare no conflicts of interest.

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