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RAPID COMMUNICATION

Grip Strength Impairment and Neuropathic-Like Pain as Predictors of Functional Decline in Hand Osteoarthritis

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Objective: (1) To define the factors associated with pain, functional limitation, grip strength (GS), sarcopenia and quality of life (QoL) in hand osteoarthritis (HOA) patients and (2) to compare the characteristics of HOA patients with or without neuropathic-like pain.

Methods: The clinical parameters (numeric rating scale (NRS) for pain, Functional Index for HOA (FIHOA), GS, QoL, and sarcopenia) were completed by hand radiographs and biological analysis. A neuropathic-like pain was retained if the DN4 score was ≥4/10. We performed a cross-sectional study comparing the patients' characteristics using the Student's *t*-test or Chi-square. The relation between clinical parameters and others was studied with Spearman correlation or logistic regression.

Results: 110 hOA patients (mean age of 66.2 years and 89% of women) were included. Twenty-eight HOA patients presented a comorbidity (25.7%: 28/109) and eight had sarcopenia (8/63: 12.7%). Hand GS was negatively associated with age (r=−0.23; p=0.049), higher in men (p=0.003), and lower in erosive disease (p=0.03). Sarcopenia significantly correlated with higher pain intensity (p=0.046), greater functional impairment (FIHOA, p=0.01), and lower QoL (p=0.03). The presence of comorbidity altered the QoL (p=0.047). Depression was significantly associated with all clinical parameters, except GS. Sixty HOA patients had neuropathic-like pain (56.0%); these were younger, had a higher FIHOA, and reported more night awakening and morning stiffness; however, C-reactive protein (CRP) levels were not different.

Conclusion: Neuropathic-like pain and sarcopenia exacerbate functional decline in HOA, highlighting the need for targeted interventions beyond conventional analgesics.

Keywords: hand osteoarthritis, neuropathic-like pain, grip strength, sarcopenia

Introduction

Osteoarthritis (OA) is the most frequent musculoskeletal disease in rheumatology. Symptoms in hand OA (HOA) patients are very like those of rheumatoid arthritis patients: pain, functional limitation, and reduced quality of life (QoL).[1] The decreased grip strength (GS) found in HOA patients reflects the radiographic severity of HOA in women and was only associated with comorbidities in men.[2] A decrease in GS can detect the existence of sarcopenia, which is defined by a decrease in muscle mass and strength.[3,4] Sarcopenia was reported to predispose to the development of mobility limitations, to increase the risk of falls and fractures and to promote dependence in the elderly.[5,6] The diagnosis of sarcopenia is therefore important in OA patients. Several studies concluded that sarcopenia increased the risk of OA or impaired function and quality of life in OA patients, especially in knee and hip,[7,8] but also in HOA.[9] Sarcopenia was also associated to more severe HOA.[10] The diagnosis of sarcopenia can be done using dual-energy X-ray absorptiometry (DEXA) or bioelectrical impedance analysis (BIA) in addition to the results of GS.[11,12] About ten years ago, a screening tool was created, the SARC-F questionnaire that makes it possible to detect sarcopenia in case of a score higher than or equal to 4.[13,14]

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Different phenotypes are reported in HOA patients.[15,16] Some are more inflammatory, especially related to adipose tissue or metabolic syndrome and low-grade inflammation.[17] Authors concluded that metabolic syndrome correlated with increased pain in HOA, independent of structural damage and anxiety/depression, underscoring its systemic impact on OA-related pain. The characteristics of pain also differ between OA patients, and neuropathic-like pain, including burning, stinging, and electric shocks, may be found in up to 50% of OA patients.[18] Neuropathic pain can contribute to the painful experience of OA, although the specific nerve damage to the somatosensory system is not yet clearly identified, hence the term 'neuropathic-like pain" used in OA.[19] Patients with OA-related pain also have altered pain thresholds in terms of pain sensitization assessed by quantitative sensory testing (QST).[20,21] Neuroimaging evidence suggests that this central sensitization phenomenon may be associated with disruption of central pain inhibition pathways.[22,23] Sensitization has also been found to be associated with brain changes beyond regions strictly dedicated to pain processing, with enhanced activity in general non-nociceptive sensory brain.[24] This neuropathic-like characteristic of pain may explain why traditional analgesics are not very effective in OA, as neuropathic pain is poorly relieved by conventional analgesics.[25] We can also suppose that the characteristics of HOA patients with neuropathic-like pain are different from those with nociceptive pain. However, to our knowledge, only one study previously compared these two HOA populations.[26]

Our cross-sectional study of HOA patients had two objectives: (1) to define the factors associated with pain, functional limitation, GS, sarcopenia, and QoL and (2) to compare the characteristics of patients with neuropathic-like and non-neuropathic pain.

Method

Ethics Statement

Ethical approval for this study was obtained from the local Ethics Committee (IRB00013412, "CHU de Clermont Ferrand IRB #1", IRB number 2023-CF108). This study complies with the principles of the Declaration of Helsinki.[27]

Informed Consent

Patients were informed about the objectives of the study, the modalities of anonymization of their personal data using the RedCap secure web platform and gave their informed consent before starting the study.

Study Design

This monocentric cross-sectional study was offered to HOA patients regularly followed in the Rheumatology Department of the University Hospital of Clermont-Ferrand.

Patients

Inclusion criteria were as follows: adult patient with HOA according to American College of Rheumatology (ACR) criteria with ≥ 2 symptomatic joints among proximal/distal interphalangeal joints or 1st interphalangeal joint with Kellgren–Lawrence (KL) ≥ 2; or symptomatic thumb base OA with KL ≥ 2.[28] Exclusion criteria were refusal to participate, inability to understand or complete the surveys in French or to express consent. Patients with destructive arthritis (rheumatoid arthritis, psoriatic arthritis, gout) were also excluded.

Demographic and Clinical Data Collection

The following parameters were collected for each included patients:

- Age, sex, tobacco use.
- Presence of diabetes, blood hypertension, or dyslipidaemia.
- The assessment and search of comorbidities was done first asking specific questions to HOA participants and second reading the file of each included patients. A comorbidity was first retained in the event of a positive response by the patient to the question of a personal history of cancer, cardiovascular disease, diabetes,

neurological disease, or severe depression. Second, in the case of a patient who did not know or could not answer with certainty, a comorbidity was retained in the event of the presence of this history in his medical record.

- We calculated the 10-year risk of fatal and non-fatal cardiovascular events using Systematic COronary Risk Evaluation (SCORE2 and SCORE2-OP) algorithm scores.[29]
- General physical examination (height, weight, blood pressure, and abdominal circumference). We calculated the body mass index (BMI) and defined the presence of metabolic syndrome according to classification criteria.[30]
- Examination of the hands: number of painful joints, synovitis, morning stiffness, and night awakening.
- GS of each hand using a Jamar hydraulic hand dynamometer. Each measurement was performed in a calm, seated and well-settled patient after explanation of the test by an experienced nurse (FF, MHS or MR). We recorded the best result of three tests for each hand and defined the maximal GS.
- General treatments (lipid-lowering, antihypertensive), analgesics, and anti-inflammatory treatments.
- Outcomes and questionnaires self-assessed by the patient including:
  - Numeric rating scale (NRS) for hand pain. NRS pain score was expressed by the patient itself. Patients rated the degree of pain they feel on a 11-point scale. Zero is no pain, the 1–3 level is mild pain, the 4–6 level is moderate pain, and the 7–10 level is high pain. Ten corresponded to the highest pain intensity.[31]
  - NRS for QoL. Patients rated the degree of QoL they feel on a 11-point scale. Zero is the lowest degree of QoL and ten corresponded to the highest and best degree of QoL.
  - DN4 questionnaire to define the presence of neuropathic pain with a score ≥ 4.[32]
  - Hand function using the Functional Index for HOA (FIHOA). FIHOA is a 10-item self-report questionnaire. Items are scored on a 4-point scale from 0 (possible without difficulty) to 3 (impossible). The scores for each item are summed to give a total score, which ranges from 0 to 30. Low scores indicate better hand function.[33]
  - Anxiety and depression using the Hospital Anxiety and Depression Scale (HAD).[34] Seven questions relate to anxiety and seven to depression, resulting in tow scores (maximum score for each=21).
  - The SARC-F scoring used as a screening test to predict patients with sarcopenia: a score higher than 4 was used to detect the patients with sarcopenia.[35] And then we used hand grip strength to confirm probable sarcopenia (cutoff values of hand grip strength, under that the presence of sarcopenia can be retained, is 27 kg in men and 16 kg in women), as already reported elsewhere.[36]

Radiological and Biological Data Collection

We verified the inclusion criteria using recent hand radiographs (less than a year old) (ie, a Kellgren-Lawrence score ≥ 2), and concluded whether metacarpophalangeal, proximal interphalangeal, or distal interphalangeal joint erosions were present. In a recent blood sample (less than three months old), we measured C-reactive protein (CRP), total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, glycaemia, and uric acid.

Statistical Analysis

Statistical analysis was performed using Stata software (version 13, StataCorp, College Station, USA). Continuous variables are presented as mean and standard deviation, subject to the normality of their distribution (Shapiro–Wilk test). Cases of non-normality are presented as medians, quartiles, and extreme values. Categorical variables are expressed as numbers and associated percentages. The comparisons of patient characteristics according to the type of pain were performed using the Student's *t*-test, Fisher's test, or the Chi-square test. The relation between pain, GS, FIHOA, SARC-F score, QoL, and the other parameters was studied by Spearman correlation test for continuous variables or by logistic regression for categorical variables. When logistic regression was not possible, we used the Student's *t*-test or Fisher's test for mean comparison. The primary analysis was completed by a multivariable regression models to adjust for confounders (eg, age, depression) and covariates determined regarding clinical relevance (age, SARC-F, FIHOA, HAD). A p-value < 0.05 was considered significant.

Results

Demographics and Clinical Characteristics

A total of 110 hOA patients, who visited the rheumatology department between May 2021 and June 2024, were included. Our sample had a mean age of 66.2 ± 9.2 years with a significant majority of women (89%). Twenty-eight HOA patients presented a comorbidity (25.7%: 28/109). Mean NRS pain was 5.3 ± 2.0 with 56% of patients (n=60) having neuropathic-like pain; NRS QoL was 6.2 mm. Mean hand GS and SARC-F scores were 13.3 ± 7.9 kg and 2.5 ± 1.7, respectively. The eight patients with SARC-F > 4 had sarcopenia according to their GS values (8/63: 12.7%). Only nine patients had clinical synovitis but more than half reported night awakening and 56% morning stiffness with a median duration of 20 minutes [Min-max: 5–120]. Erosive disease was present in 24% (n=22) of patients. The median CRP level was 1.6 mg/l [min-max: 0.6–14.7]. Around 40% were taking analgesics and 18% NSAIDs; four patients were being treated with methotrexate but none were taking hydroxychloroquine.

Factors Associated with Clinical Parameters

The results of the association between HOA patient characteristics and clinical parameters are presented in Table 1. Depression, measured by the HAD-D scale, was significantly associated with all clinical parameters, except GS. The association was positive with NRS pain, SARC-F, and FIHOA and negative with QoL. NRS pain was negatively associated with HDL cholesterol levels and positively with triglycerides. Except for depression, FIHOA was not significantly associated with any parameters. GS was negatively associated with age and SCORE2 and positively with uric acid levels. Men had a higher GS than women (20.1 ± 13.2 versus 12.3 ± 6.3 kg; p=0.003) and erosive disease was associated with a lower GS (9.5 ± 4.5 versus 13.6 ± 6.4 kg; p=0.03). The QoL was significantly negatively impacted by

Table 1 Association of Characteristics with Clinical Parameters

	NRS pain	FIHOA	Grip strength	QoL	SARC-F
Age	r=−0.15 p=0.13	r= −0.04 p=0.70	**r=−0.23 p=0.049**	r= −0.03 p=0.78	r=0.16 p=0.23
Men	p=0.32*	p=0.89*	**p=0.003***	p=0.88*	p=0.28*
Tobacco	OR=0.22 [0.02–2.74]	p=0.62*	p=0.22*	p=0.17*	p=0.65*
Comorbidity	p=0.42*	p=0.70*	p=0.89*	**p=0.047***	OR=0.5 [0.11–2.66]
SCORE2	r=−0.04 p=0.71	r=0.09 p=0.37	**r=- 0.27 p=0.02**	r=−0.16 p=0.14	r=0.09 p=0.50
BMI	r=0.18 p=0.06	r=0.02 p=0.98	r=0.13 p=0.26	r= −0.20 p=0.06	**r=0.31 p=0.01**
Abdominal circumference	r=0.02 p=0.81	r= −0.03 p=0.80	r=0.11 p=0.32	r= −0.19 p=0.14	**r=0.45 p=0.005**
Systolic BP	r=0.07 p=0.46	r=0.06 p=0.80	r= −0.10 p=0.40	r=0.01 p=0.90	r= −0.14 p=0.29
Diastolic BP	r=0.13 p=0.19	r=0.02 p=0.85	r=0.14 p=0.25	r=0.04 p=0.75	r=0.02 p=0.90
Metabolic syndrome	OR=0.42 [0.03–6.95]	p=0.13*	p=0.34*	p=0.16*	OR=3.2 [0.35–28.7]
Arthralgia	OR=4.6 [0.4–52.4]	OR=4.4 [0.39–50.4]	p=0.91*	p=0.86*	OR=0.37 [0.04–3.34]
Synovitis	p=0.06*	p=0.38*	p=0.52*	p=0.17*	p=0.61*
Night awakening	OR=2.3 [0.2–26.2]	OR=2.3 [0.2–26.4]	p=0.47*	p=0.59*	OR=3.0 [0.54–16.8]
Morning stiffness	OR=1.4 [0.08–22.3]	OR=2.8 [0.25–32.7]	p=0.99*	p=0.81*	OR=0.22 [0.02–1.96]

(*Continued*)

Table 1 (Continued).

	NRS pain	FIHOA	Grip strength	QoL	SARC-F
FIHOA	r=0.25 p=0.01				
Hand grip	r= −0.002 p=0.98	r= - 0.18 p=0.15			
HAD-A	r= 0.06 p=0.54	r=0.03 p=0.77	r= −0.18 p=0.13	r= −0.18 p=0.08	r=0.08 p=0.54
HAD-D	**r=0.2 p=0.045**	**r=0.33 p<0.001**	r=−0.19 p=0.12	**r= −0.31 p=0.003**	**r=0.43 p<0.001**
QoL	r=−0.17 p=0.11	r= −0.19 p=0.07	r= −0.11 p=0.40		
SARC-F	**r=0.25 p=0.046**	**r=0.32 p=0.01**	r= −0.25 p=0.14	**r =−0.28 p=0.03**	
Erosive radiographs	OR=0.62 [0.05–7.16]	p=0.87*	**p=0.03***	p=0.14*	OR=1.71 [0.18–16.18]
CRP	r=0.14 p=0.15	r=0.16 p=0.13	r=0.02 p=0.85	r= −0.11 p=0.29	r=0.03 p=0.83
Total cholesterol	r= −0.20 p=0.036	r= −0.03 p=0.79	r= −0.02 p=0.84	r=0.08 p=0.47	r= −0.21 p=0.11
LDL cholesterol	r= −0.16 p=0.10	r= −0.07 p=0.49	r= −0.08 p=0.50	r=0.07 p=0.54	r= −0.16 p=0.25
HDL cholesterol	**r= −0.23 p=0.02**	r= −0.11 p=0.27	r= −0.003 p=0.98	r=0.05 p=0.63	r= −0.23 p=0.07
Triglycerides	**r=0.21 p=0.036**	r=0.14 p=0.18	r=0.14 p=0.24	r= −0.14 p=0.19	r=0.09 p=0.50
Glycemia	r= 0.04 p=0.67	r=0.15 p=0.16	r=0.06 p=0.62	r= −0.15 p=0.19	r=0.10 p=0.45
Uric acid	r=0.002 p=0.98	r= −0.02 p=0.86	**r=0.27 p=0.03**	r= −0.09 p=0.43	r= −0.20 p=0.15

Notes: *Mean comparison by the Student's *t*-test when logistic regression is not possible. r: correlation coefficient; p= p-value; OR: odds ratio; BMI: body mass index; BP: blood pressure; NRS: numeric rating scale; FIHOA: Functional index for hand osteoarthritis; HAD: Hospital Anxiety and Depression Scale; QoL: Quality of Life; CRP: C-reactive protein; LDL: Low-density lipoprotein; HDL: high-density lipoprotein; SCORE2: Systematic COronary Risk Evaluation version 2. Bold values are statistically significant.

depression, comorbidity, and sarcopenia. SARC-F scores (1.9 ± 0.7 men versus 2.6 ± 1.7 women; p=0.28) and the number of patients with sarcopenia (1/8 men (12.5%) versus 7/55 women (12.7%); p=0.73) did not differ according to sex. SARC-F was positively associated with BMI and abdominal circumference. Multivariable regression analyses to adjust for confounders (eg, age, depression) did not find anymore significant associations between NRS pain, GS, QoL and SARC-F and the other parameters.

Comparison of Patients with or without Neuropathic-Like Pain

In our cohort of 110 hOA patients, 60 (56%) had neuropathic-like pain. Table 2 summarises the comparison of characteristics between patients with or without neuropathic-like pain. The only difference detected regarding general characteristics was that patients with neuropathic-like pain were younger. They reported more night awakening and morning stiffness but the pain intensity was similar between groups. In contrast, FIHOA was higher in the neuropathic-like pain group. There were no other differences between groups, including the frequency of erosive radiographs, tender joint counts, GS, or QoL.

Discussion

We found that hand GS was negatively associated with age and SCORE2. Haugen et al also reported a negative association between GS and a higher comorbidity index.[37] Therefore, it seems important to ask HOA patients about their previous history to search for comorbidities. Siviero et al concluded that comorbidity was definitively and independently

Table 2 Comparison of Characteristics Between HOA Patients with or without Neuropathic-Like Pain

Characteristics	Number of HOA patients		p-value
	with neuropathic-like pain DN4+ (n=60)	Without neuropathic-like pain DN4- (n=50)	
Age, years	64.1 ± 8.3	67.8 ± 8.9	**0.03**
Female	54/60 (90.0%)	41/47 (87.2%)	0.65
Tobacco	6/56 (10.7%)	5/44 (11.4%)	0.92
Comorbidity	14/59 (23.7%)	8/47 (17.0%)	0.40
Charlson score	2.3 ± 1.2	2.6 ± 1.4	0.28
Heart SCORE2, %	5.6 ± 3.7	6.2 ± 3.3	0.38
BMI	26.3 ± 5.8	26.0 ± 4.7	0.78
Abdominal circumference, cm	89.6 ± 13.9	90.4 ± 11.3	0.80
Systolic BP, mmHg	136.9 ± 17.2	137.0 ± 16.3	0.97
Diastolic BP, mmHg	80.6 ± 11.3	77.2 ± 7.1	0.08
Metabolic syndrome	17/57 (29.8%)	12/42 (28.6%)	0.89
NRS pain, cm	5.6 ± 2.0	5.0 ± 2.0	0.12
Arthralgia	44/59 (74.6%)	28/45 (62.2%)	0.18
Synovitis	7/59 (11.9%)	2/45 (4.4%)	0.29
Night awakening	40/58 (69.0%)	15/45 (33.3%)	**<0.001**
Morning stiffness	35/46 (76.1%)	16/42 (38.1%)	**<0.001**
FIHOA	11.7 ± 5.9	8.5 ±6.0	**0.008**
Grip strength, kg	13.5 ± 9.1	13.5 ± 6.3	0.97
HAD-A	9.2 ± 3.7	8.5 ± 3.7	0.33
HAD-D	6.3 ± 4.0	5.5 ± 3.8	0.31
QoL, cm	6.2 ± 1.8	6.3 ± 1.9	0.77
SARC-F	2.5 ± 1.8	2.4 ± 1.7	0.83
Erosive Radiographs	14/52 (26.9%)	8/40 (20.0%)	0.44
CRP, mg/l	2.8 ± 2.8	2.4 ± 2.3	0.39
Total cholesterol, g/l	2.30 ± 0.37	2.15 ± 0.46	0.09
LDL cholesterol, g/l	1.43 ± 0.38	1.31 ± 0.41	0.13
HDL cholesterol, g/l	0.64 ± 0.15	0.64 ± 0.22	0.81
Triglycerides, g/l	1.18 ± 0.54	1.10 ± 0.64	0.48
Glycaemia, mmol/l	5.38 ± 1.02	5.28 ± 1.00	0.65
Uric acid, µmol/l	285 ± 73	296 ± 80	0.51

Note: Values are mean ± standard deviation or number of patients and percentage. Bold values are statistically significant.
Abbreviations: HOA, hand osteoarthritis; DN4, douleur neuropathique 4; BMI, body mass index; BP, blood pressure; NRS, numeric rating scale; FIHOA, Functional index for hand osteoarthritis; HAD, Hospital Anxiety and Depression Scale; QoL, Quality of Life; CRP, C-reactive protein; LDL, Low-density lipoprotein; HDL, high-density lipoprotein; SCORE2, Systematic COronary Risk Evaluation version 2; kg, kilogram; cm, centimeters; g/l, gram per liter.

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associated with hand functional limitation, however, it did not affect the association of HOA with physical function.[38] Our results found that erosive disease caused a significant decrease in GS. It is now well-known that erosive disease is more severe in more symptomatic and inflammatory patients with worse hand function. Tan et al found that decreased GS reflected the radiographic severity of HOA, especially in women.[2] They performed a sex-stratified GS analysis due to this interaction between GS and sex and found different results according to sex for GS-associated factors. We could not perform the same analysis as the low number of men (n=12) in our cohort did not permit any statistically relevant comparisons. Finally, we noticed a positive association between GS and uric acid levels. Covello et al had already reported an association between gout and sarcopenia, which is still debated; the mean uricemia in our study was normal.[39]

Moradi et al found that erosive HOA was associated with sarcopenia, however, only in patients without concomitant knee OA, which could correspond to patients with a more inflammatory phenotype.[10] In our study, sarcopenia, detected by SARC-F, was associated with a worse clinical profile, ie, increased pain intensity, increased functional limitation, and reduced QoL. However, we did not find any association between SARC-F and CRP levels, synovitis, or radiographic erosions. Moreover, the lack of association between SARC-F and GS could imply that GS measurement to conclude sarcopenia is not relevant in HOA because of bias due to pain. The detection of sarcopenia for its prevention and management seems, nonetheless, important in OA patients. Sarcopenia is now well-recognized as a central risk factor of frailty in the elderly and is associated with functional impairment, physical disability, and an increased risk of falls.[40] Preventing sarcopenia is important in OA management to limit this risk of falling in the elderly OA population, which is often also osteoporotic. Using SARC-F questionnaire to detect sarcopenia in OA patients can be useful because it is easy to do in everyday routine care. By the same way, Lovett et al proposed to use SARC-F questionnaire to detect sarcopenia in hip OA patients undergoing potential hip replacement. These patients at risk of sarcopenia will be more likely to be referred to orthopedic surgery to undergo arthroplasty before the onset of sarcopenia or to fight preoperatively against the decrease in muscle mass in order to reduce postoperative complications related to sarcopenia.[41–43] However, SARC-F is not sufficient to conclude to sarcopenia and complementary methods like BIA or body composition measured by DEXA are necessary to strengthen and confirm the sarcopenia definition, but this requires more time than simply filling a questionnaire and investing in the purchase of equipment.

Patients with neuropathic-like pain were younger and had a higher FIHOA, which corresponded with higher functional limitations. Gloersen et al concluded that peripheral and possibly central sensitization were associated with impaired function, finding that the pressure pain threshold was associated with a greater GS.[44] In our study, we found no difference in GS between HOA with or without neuropathic-like pain. We noticed more inflammatory pain with more night awakening and morning stiffness in HOA patients with neuropathic-like pain, yet no differences in CRP levels between these patients. Neuropathic pain is not related to systemic inflammation but rather to low-grade inflammation and/or neuroinflammation.[45] This may explain the lack of difference in CRP levels detected in our study. We used the DN4 tool to define neuropathic pain in our sample of HOA patients.[32] We can raise concerns about the applicability of the DN4 tool in HOA populations. In our experience, filling DN4 causes no difficulty for OA patients with HOA or OA from another location or other rheumatic diseases.[46] Then, it is up to the medical doctor in charge of the patient to define whether the neuropathic pain is of local or general etiology. A local cause may benefit from the application of capsaicin or lidocaine, while a general cause may be treated with antiepileptics or antidepressants.[47]

In our cohort, most HOA patients had no analgesic or anti-inflammatory treatment. This could be due to an average pain intensity level but also to the lack of efficacy of traditional analgesics in neuropathic-like pain. Van der Meulen et al found that neuropathic-like pain in HOA was resistant to prednisolone therapy.[26] In contrast, anti-neuropathic and centrally acting analgesics, such as pregabalin or duloxetine, were efficient in decreasing the NRS pain in 65 hOA patients.[48] Similarly, we found that local application of 8% capsaicin patches reduced the pain intensity in 6/8 hOA patients with neuropathic-like pain.[49] It is therefore very important to clearly define the type of pain and to identify the presence of neuropathic-like pain in OA patients in order to choose an appropriate and effective analgesic treatment. In fact, in OA studies, pain described as neuropathic could be also nociplastic.[50] Nociplastic pain involves central sensitization due to changes in the nervous system (plasticity). Tools exist to specify the different pain phenotypes in OA. We used the DN4 tool, but the PainDETECT has also been used in the APPROACH cohort to distinguish patients

with nociceptive pain from those with neuropathic pain that can therefore also be considered as nociplastic.[51] A PainDETECT score higher than 13 leads to the conclusion of probable neuropathic pain and a score higher that 19 to certain neuropathic pain. QST measuring pain thresholds is used to identify the pain sensitization process, which is involved in the phenomenon of diffuse pain in OA.[21] However QST only provides indirect evidence about the brain's involvement in OA-related pain. In recent years, neuroimaging studies have therefore developed, and particular in brain functional MRI. Several neuroimaging studies have shown that the neuronal and glial elements of the sensory cortex, hypothalamus and midbrain exhibit changes in OA patients that may modulate afferent nociceptive signals and contribute to chronic OA-related pain.[52] The use of brain functional MRI is not yet possible routinely in the management of pain of OA patients, but in the near future it will make it possible to better define the type of pain in order to best adapt the analgesic treatment.[53]

Our study has some limitations. First, the number of HOA patients included might be considered low compared with some cohorts. Moreover, the absence of sample size calculation could raise concerns about adequate statistical power. Nevertheless, compared with other cross-sectional studies, we have included the same number of patients or more. Few studies have assessed the factors associated with clinical outcomes (eg, GS or sarcopenia) in HOA and compared them against the characteristics of HOA patients with or without neuropathic-like pain. Second, this is a monocentric study, which can limit the generalisation of our results. For example, only 24% of our sample had erosive disease, which might be lower than expected in HOA patients followed at a University Hospital. This proportion was, however, sufficient to draw relevant comparisons between erosive and non-erosive patients. Using GS alone for sarcopenia assessment was also a limitation. Incorporating complementary methods like BIA to assess sarcopenia would have strengthened the sarcopenia definition and the robustness of our results.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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