



Patterns and natural history of hand pain in individuals with symptomatic hand osteoarthritis in a prospective cohort study: A post-hoc analysis of a randomised controlled trial



Mahnuma Mahfuz Estee, Yuanyuan Wang, Yuan Z. Lim, Anita E. Wluka, Flavia M. Cicuttini*

School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC 3004, Australia

ARTICLE INFO

Handling Editor: Professor H Madry

Keywords:

Hand osteoarthritis
Hand pain
Phenotype
Natural history

ABSTRACT

Objective: To investigate the variation in the distribution and the natural history of hand pain over 6 weeks in individuals with symptomatic hand osteoarthritis.

Design: Patient-reported outcome data were collected at baseline and weekly for 6 weeks from community-based participants enrolled in a randomised controlled trial. Participants were grouped based on location of significant pain (Visual Analogue Scale, $VAS \geq 40/100$ mm) (both carpometacarpal (CMC) and interphalangeal (IP), CMC only, and IP only).

Results: At baseline, of the 106 participants, 55(51.9 %) had pain in both CMC and IP joints, 28(26.4 %) in IP joints only, and 16(15.1 %) in CMC joint only. Those with CMC and IP pain had significantly higher VAS pain [68.1 (2.6) vs 59.3 (3.5) vs 51.2 (4.7)]; Australian Canadian Osteoarthritis Hand Index, (AUSCAN) pain [290.1 (15.7) vs 225.3 (21.2) vs 237.9 (28.4)], stiffness [57.1 (3.7) vs 44.6 (5.0) vs 32.2 (6.7)] and functional limitation [527.5 (30.9) vs 356.0 (41.7) vs 433.3 (55.7)]; and pain sensitization [PainDETECT score 11.1 (1.1) vs 8.1 (1.8) vs 5.8 (1.9)] compared to those with IP or CMC only pain, respectively. All groups showed improvement in outcomes over 6 weeks without significant inter-group differences.

Conclusion: In a population with significant hand pain, pain in both CMC and IP joints was most common and identified a more severe phenotype than pain in IP or CMC only with higher pain, more functional limitation and pain sensitization. These data have the potential to inform clinical management of patients with hand pain and patient selection in clinical trials.

1. Background

Hand osteoarthritis (OA) causes disabling hand pain, functional impairment and reduced quality of life [1]. The incidence of hand OA has doubled in the last three decades [2] and hand OA is ranked the second cause of years of life lost due to disability among those with OA after knee OA [3]. Hand OA is a heterogeneous condition that commonly affects multiple hand joints and different joint groups [4]. Effective treatments are limited for hand OA, with efficacy further impeded by the complexity of this condition with multiple phenotypes [5]. It is important to understand the course and impact of different phenotypes in order to inform appropriate therapy and provide patients with information regarding disease prognosis [6]. There is a need to better understand the different clinical phenotypes of hand OA in order to develop targeted and effective treatment strategies.

Hand OA phenotypes are not well defined. The American College of Rheumatology (ACR) has established classification criteria for hand OA based on clinical findings [7]. However, the ACR criteria have limitations, including not considering all the joints of the hand or functional impairment as a major criterion to diagnose hand OA or early stage of disease [8,9]. Osteoarthritis Research Society International (OARSI) and the European League Against Rheumatism (EULAR) have described phenotypes of hand OA: interphalangeal (IP) OA with/without nodal involvement, thumb base OA (primarily trapeziometacarpal joint) with/without IP OA, and erosive OA [6,8]. Radiographically, three different patterns of hand OA are also observed: finger OA, thumb OA, and combined thumb and finger OA [10]. However, the association between radiological hand OA and clinical manifestations is inconsistent and there is chance of underdiagnosis of hand OA in younger population or symptomatic hand OA [11,12].

* Corresponding author. School of Public Health and Preventive Medicine, Monash University, 553 St Kilda Road, Melbourne, VIC 3004, Australia.

E-mail addresses: Mahnuma.estee1@monash.edu (M.M. Estee), yuanyuan.wang@monash.edu (Y. Wang), yuan.lim@monash.edu (Y.Z. Lim), anita.wluka@monash.edu (A.E. Wluka), flavia.cicuttini@monash.edu (F.M. Cicuttini).

<https://doi.org/10.1016/j.ocarto.2023.100413>

Received 28 June 2023; Received in revised form 28 September 2023; Accepted 15 October 2023

2665-9131/© 2023 The Author(s). Published by Elsevier Ltd on behalf of Osteoarthritis Research Society International (OARSI). This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Phenotyping of hand OA is important to consider as different phenotypes may differ in risk factors, disease course, clinical burden and management options [4]. Current options for phenotyping based on presence of OA diagnosed with ACR criteria/radiographic assessment have the potentiality to exclude sub-groups and combine others. Therefore, phenotyping based on location of significant hand pain could be clinically relevant and less restrictive. Previous studies have described the characteristics of phenotypes based on the site of clinical hand pain in selective populations in clinical settings, such as GP/specialist clinic or inpatient/outpatients from the rehabilitation and rheumatology department [13,14]. Although joint pain is a key reason for hand OA patients to seek help, there is limited data on the patterns and natural history of hand pain in community-based populations.

Therefore, the aim of the current study was to examine: (1) the patterns and variations in the distribution of hand pain and their association with hand pain and function; and (2) the natural history of hand pain over 6 weeks based on different patterns of hand pain in community-based individuals with symptomatic hand OA participating in a clinical trial.

2. Methods

2.1. Study participants

This cohort study examined participants who took part in a randomised controlled trial examining the effect of topical Diprosone OV (betamethasone dipropionate in Optimised Vehicle) in hand OA, conducted between May 2020 and May 2022 in Melbourne Australia (ACTRN12620000599976) [15]. Ethics approval was obtained from the Alfred Hospital Ethics Committee (117/20) and Monash University Human Research Ethics Committee (24219). All participants provided written informed consent.

The participants were recruited from the community via advertisements through local and social media, and from medical practitioners. Participants aged 40 years or more with a hand pain score of ≥ 40 on a 100 mm visual analogue scale (VAS) and radiologic OA (Kellgren and Lawrence grade ≥ 2) in at least one joint were recruited [16]. Those with other joint conditions apart from OA or any contraindication in Diprosone OV ointments were excluded. Details of the inclusion and exclusion criteria were described in the protocol paper [17]. Participants were randomly allocated to apply either Diprosone OV or placebo (plain paraffin ointment) to painful joints 3 times daily for 6 weeks.

2.2. Demographic data

At baseline, data on age, gender, height and weight were collected using a questionnaire, and BMI was calculated.

2.3. Patient-reported outcomes

Hand pain and function were assessed using validated questionnaires at baseline and 6 weeks. General hand pain was measured using Visual Analogue Scale (VAS) (0–100) [18] and the Australian Canadian Osteoarthritis Hand Index (AUSCAN) pain (0–500) scale [19]. Individual joint pain was assessed using VAS (0–100) for 4 distal IP (DIP) joints, 4 proximal IP (PIP) joints, 5 metacarpophalangeal (MCP) joints, and IP and carpometacarpal (CMC) joint of the thumb. AUSCAN function subscale (0–900) [19] and Functional Index for Hand OA (FIHOA)(0–30) [20] were used for assessing the functionality of the hand. Data on AUSCAN stiffness subscale (0–100) [19], and PainDETECT questionnaire (PDQ, to assess neuropathic-like pain) (0–38) [21] were also collected. PDQ scores ≥ 13 were considered as possible neuropathic-like pain, and PDQ scores ≥ 19 considered as probable neuropathic-like pain [21]. Weekly general hand pain and individual joint pain were assessed using a 0–10 numeric rating scale (NRS).

2.4. Radiographic assessment

X-ray using the standardized posteroanterior view of the symptomatic hand was performed at baseline. Osteophyte and joint space narrowing were assessed for IP and CMC joints using the OARSI atlas by an experienced observer [22], and the presence and severity of radiologic OA were assessed based on the Kellgren and Lawrence grade (KL grade) [16].

2.5. Study hand selection

The hand with a higher general VAS at baseline was selected as the study hand. When the general VAS score was equal for both sides, the dominant hand was selected as the study hand.

2.6. Statistical analysis

Data were presented as for study hand as mean (SD) or number (percentage). Average IP pain (0–100) was calculated using the sum of all distal IP, proximal IP and thumb IP scores divided by 9. Hand joints with ≥ 40 out of 100 in VAS at baseline were considered as having significant pain.

Three groups were defined based on the location of significant pain. Those who had significant pain only at IP joints but not CMC joint in the study hand were considered as the IP only pain group. Those who had significant pain only at CMC joint but not IP joints were considered as the CMC only pain group. Those who had significant pain at both IP and CMC joints were considered as the CMC and IP pain group.

The change in patient-reported outcome scores was calculated by subtracting the baseline score from the follow-up score. Percentage change was calculated as change in score $\times 100$ /baseline score. 30% and 50% improvement were calculated if the % change for the individual scale was ≤ -30 and ≤ -50 . For the study hand, the maximum IP KL grade was defined as the maximum KL grade among the 9 IP joints (4 DIP, 4 PIP and 1 thumb IP).

General linear model and chi square test were used to examine the differences among the three groups. Post-hoc between group difference was examined using Bonferroni test. A total burden of hand pain score was calculated each of the 3 group (IP and CMC, IP only, CMC only) by summing the VAS for pain at each time point from baseline to 6 weeks. The original RCT examining the effect of topical corticosteroid on hand pain and function showed no effect [15]. So, we examined the treatment group and placebo group together without adjustment for group allocation in longitudinal analysis.

A p value less than 0.05 was considered as statistically significant. Data were analysed using SPSS version 27.0 (SPSS, Chicago, Illinois, USA) and STATA version 17.0 (College station, Texas, USA).

3. Result

One hundred and six participants were included in the study. The mean general VAS pain was 61.9 (SD 19.4). Of those, 55 (51.9 %) had pain in both CMC and IP joints, 28 (26.4 %) had pain in the IP joints only, 16 (15.1 %) had pain in the CMC joint only, and 7 (6.6 %) had pain in the MCP joints only. The analyses of this study focussed on the 99 participants with significant pain in the CMC and/or IP joints, excluding those with the MCP pain only due to the small numbers of participants in this group.

The baseline characteristics of participants are described in Table 1. Age and BMI were similar across the 3 groups: those with the CMC only, IP only and both CMC and IP pain. Although not significant, the percentage of females in the CMC only group tended to be lower (75%) than in the other two groups (approximately 92%). Participants with both the CMC and IP pain had a non-significant longer duration of pain and greater number of IP joint involvement. There were significant differences among groups in terms of proportion of possible and probable neuropathic-like pain with this higher among those with both the CMC and IP pain (35.7% with possible neuropathic-like pain and 19% probable neuropathic-like pain).

Table 1
Baseline characteristics of participants in different phenotypes of Hand Pain.

Variables	Total population	CMC only	IP only	CMC and IP	P value
	N = 106	N = 16	N = 28	N = 55	
Age, years	64.2 (7.4)	63.7 (6.8)	63.4 (7.0)	64.9 (7.1)	0.60
Female	91 (85.8%)	12 (75%)	26 (92.9%)	51 (92.7%)	0.10
BMI (kg/m ²)	26.8 (4.1)	26.6 (4.4)	26 (3.2)	27.4 (4.6)	0.35
Duration of pain, years	4.4 (4.1)	3.5 (2.6)	4.0 (3.7)	4.9 (4.5)	0.42
Number of IP involved (0–9)	–	–	3.6 (2.7)	4.7 (3.2)	0.11
Possible neuropathic-like pain; PDQ \geq 13	21 (28%)	0	4 (25.7%)	15 (35.7%)	<0.05
Probable neuropathic-like pain PDQ \geq 19	8 (10.7%)	0	0	8 (19%)	<0.05
Study hand Max IP KL grade					0.001 ^a
0–1	8 (9.1%)	5 (35.7%)	0	2 (4.8%)	
2	33 (37.9%)	6 (42.9%)	7 (28%)	18 (42.9%)	
3–4	46 (52.9%)	3 (21.4%)	18 (72%)	22 (52.4%)	
Study hand CMC KL grade					0.51
0–1	25 (28.1%)	3 (21.4%)	7 (28%)	13 (29.5%)	
2	43 (48.3%)	5 (35.7%)	13 (52%)	22 (50%)	
3–4	21 (23.6%)	6 (42.9%)	5 (20%)	9 (20.5%)	

Data presented as mean (standard deviation) or number (percentage).

^a Significant difference was found between CMC pain only and IP pain only groups and CMC pain only and between CMC and IP pain groups. PainDETECT questionnaire, PDQ; Carpometacarpal joint, CMC; Interphalangeal, IP; KL Kellgren and Lawrence.

Radiological assessment showed that 72% of those with the IP only group had IP KL grade 3–4 vs 21.4% in the CMC only group and 52.4% in the CMC and IP pain group. There was no significant difference for max IP KL grade between those with both CMC and IP pain and those with IP only. 42.9% of participants with the CMC only group had CMC KL grade 3–4 vs 20% in the IP only group and 20.5% in the CMC and IP pain group. There was no significant difference for CMC KL grade for those with both CMC and IP pain and those with the CMC only pain.

The baseline pain, function, stiffness and other health outcome scores across three groups are presented in Table 2. There were significant differences among the three groups in terms of general VAS, AUSCAN pain, AUSCAN function, AUSCAN stiffness and PDQ scores. Those with both CMC and IP pain had higher scores for general VAS [mean (standard error, SE) (68.1 (2.6) vs 51.2 (3.5)], PDQ scores [mean (SE) 11.1 (1.1) vs 5.8 (1.9)] and AUSCAN stiffness [mean (SE) 57.1 (3.7) vs 44.6 (6.7)] from those with the CMC only pain. However, those with the CMC and IP pain had higher scores for AUSCAN pain [mean (SE) 290.1 (15.7) vs 225.3 (21.2)] and AUSCAN function [mean (SE) 527.5 (30.9) vs 356.0 (41.7)] compared to those with the IP only pain. These findings persisted after adjusting for age, BMI and sex. There was no significant difference in total burden of pain over 6 weeks among three groups.

Table 2
Baseline outcome scores across different patterns of Hand Pain.

Baseline data	Total	Only CMC	Only IP	CMC and IP	P	Only CMC	Only IP	CMC and IP	P
	N = 106	N = 16	N = 28	N = 55		N = 16	N = 28	N = 55	
	Unadjusted (Mean, Standard Deviation)					Adjusted ^a (Mean, Standard Error)			
Pain									
General; VAS (0–100)	61.9 (19.4)	51.6 (24.1) ^b	59.2 (18.4)	68.2 (15.8) ^b	0.003	51.2 (4.7) ^b	59.3 (3.5)	68.1 (2.6) ^b	0.01
Total pain score over the 6 weeks (0–70)	32 (12.9)	29.9 (11.1)	29.5 (11.9)	35 (13.2)	0.20	29.9 (11.1)	29.5 (11.9)	34.9 (13.4)	0.26
General, AUSCAN (0–500)	256.6 (117.9)	235.4 (126.2)	224.6 (113.2) ^c	297.7 (102.4) ^c	0.01	237.9 (28.4)	225.3 (21.2) ^c	290.1 (15.7) ^c	0.04
Average IP, VAS (0–100)	29.4 (22.2)	–	30.7 (19.2)	39 (19.8)	0.07	–	30.5 (3.8)	38.4 (2.8)	0.1
CMC, VAS (0–100)	51.7 (33.4)	67.8 (14.9)	–	73.8 (17.1)	0.20	66.0 (4.3)	–	74.7 (2.3)	0.08
Neuropathic-like pain, PDQ (0–38)	9.4 (6.8)	6.0 (3.5)	8.3 (5.3)	11 (7.7)	0.05	5.8 (1.9) ^b	8.1 (1.8)	11.1 (1.1) ^b	<0.043
Function									
AUSCAN (0–900)	454.4 (234.9)	430.0 (217.5)	353.2 (238.8) ^c	545.4 (201.7) ^c	<0.001	433.3 (55.7)	356.0 (41.7) ^c	527.5 (30.9) ^c	0.005
FIOHA (0–30)	9.5 (6.1)	8.4 (5.6)	7.8 (5.1)	10.6 (6.1)	0.10	7.8 (1.4)	8.0 (1.1)	10.2 (0.8)	0.17
Stiffness									
AUSCAN (0–200)	49.3 (28.2)	31.3 (26.2) ^c	44.1 (24.9)	59.6 (26.5) ^c	<0.001	32.2 (6.7) ^c	44.6 (5.0)	57.1 (3.7) ^c	0.004

Visual Analogue Scale, VAS; Australian Canadian Osteoarthritis Hand Index, AUSCAN; Functional Index for Hand OA, FIOHA; PainDETECT questionnaire, PDQ; Carpometacarpal joint, CMC; Interphalangeal, IP.

^a adjusted for age, BMI and sex.

^b Between group difference (Only CMC pain vs CMC and IP pain groups) was examined using Bonferroni test, $p < 0.05$.

^c Between group difference (CMC and IP pain vs only IP pain groups) was examined using Bonferroni test, $p < 0.05$.

Table 3
Change in clinical outcomes over 6 weeks in groups with different patterns of significant hand pain in the whole population.

	CMC only	IP only	CMC and IP	P value
Change in pain score (follow-up - baseline)				
General; VAS (0–100)	−14.5 (34.8)	−20 (19.2)	−22.4 (26.4)	0.57
General, AUSCAN (0–500)	−97.8 (142.8)	−69.6 (101.3)	−70.8 (117.0)	0.70
30% improvement in pain				
General; VAS (0–100)	8 (53.3%)	13 (48.1%)	26 (50%)	0.95
General, AUSCAN (0–500)	7 (46.7%)	16 (59.3%)	21 (42%)	0.35
50% improvement in pain				
General; VAS (0–100)	6 (40%)	9 (33.3%)	16 (30.8%)	0.80
General, AUSCAN (0–500)	6 (40%)	11 (40.7%)	13 (26%)	0.34
Change in Function score (follow-up-baseline)				
AUSCAN (0–900)	−139.1 (257.8)	−42.2 (195.1)	−113.9 (189.6)	0.23
FIOHA (0–38)	−1.6 (5.2)	−0.96 (3.0)	0.01 (3.8)	0.27
30% improvement in Function				
AUSCAN (0–900)	6 (37.5%)	10 (38.5%)	19 (38%)	1.0
FIOHA	7 (46.7%)	9 (34.6%)	8 (18.6%)	0.08
50% improvement in Function				
AUSCAN (0–900)	6 (37.5%)	5 (19.2%)	11 (22%)	0.36
FIOHA	5 (33.3%)	5 (19.2%)	4 (9.3%)	0.09
Change in stiffness score (follow-up-baseline)				
AUSCAN (0–200)	−9.4 (31.5)	−7.2 (18.7)	−16.2 (27.4)	0.31
30% improvement in stiffness AUSCAN (0–200)	6 (50%)	11 (42.3%)	22 (44.9%)	0.91
50% improvement in stiffness AUSCAN (0–200)	5 (41.7%)	7 (26.9%)	18 (36.7%)	0.59

Data presented as mean (standard deviation) or number (percentage).

Significance of difference was examined using General Linear Model (unadjusted) or Chi square test (unadjusted).

Visual Analogue Scale, VAS; Australian Canadian Osteoarthritis Hand Index, AUSCAN; Functional Index for Hand OA, FIOHA; Carpometacarpal joint, CMC; Interphalangeal, IP.

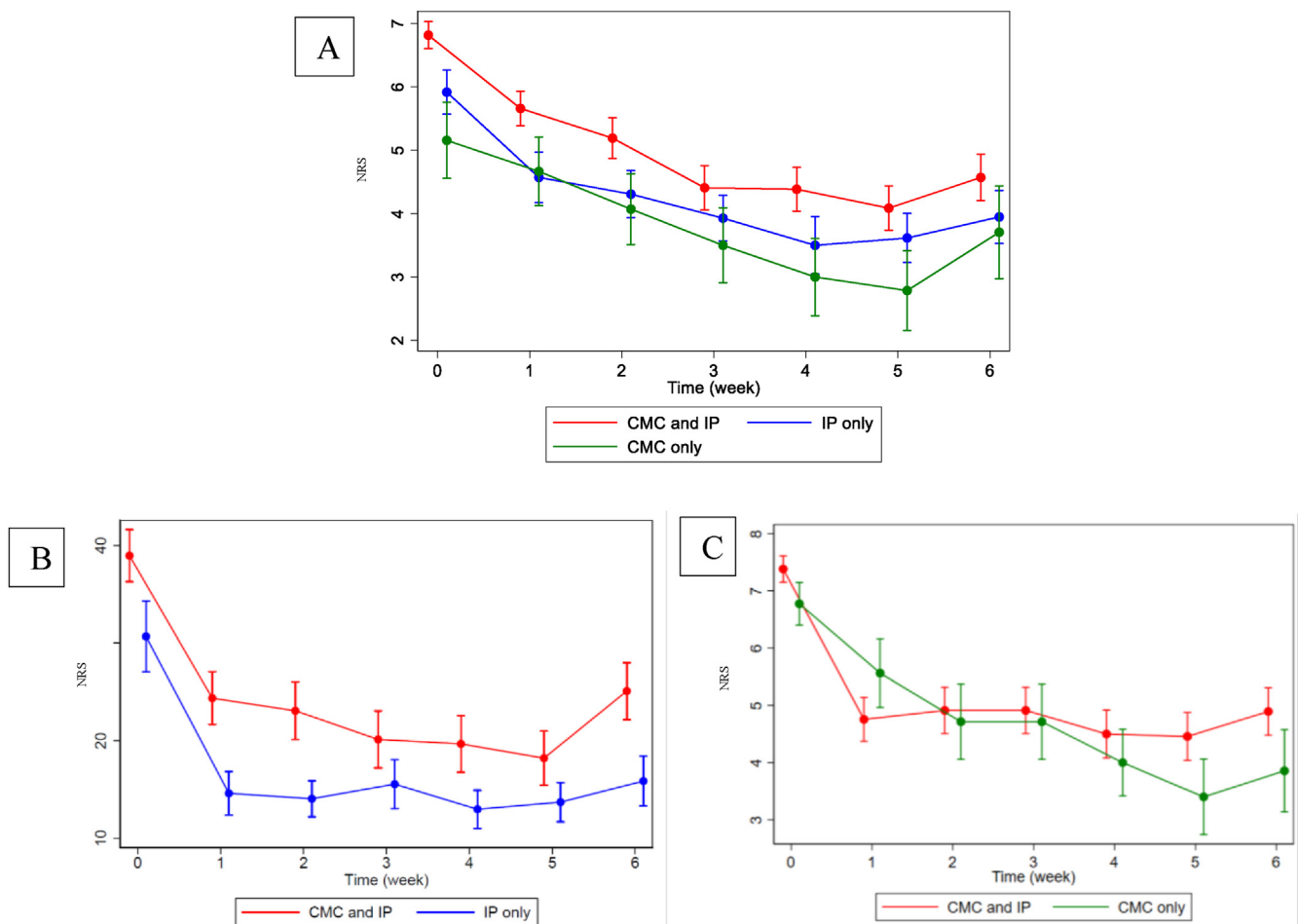


Fig. 1. Mean score of the NRS over 6 weeks in CMC only, IP only and CMC and IP pain phenotypes patients. Error bar represents SE. A) general hand pain (NRS, 0–10), B) IP pain (NRS, 0–90; as nine individual joints comprised IP joints), C) CMC pain (NRS 0–10). Red line represents pain for those with CMC and IP pain, blue lines represents those with IP pain only and green line represents those with CMC pain only.

similar pattern of pain reduction from baseline to 4 weeks. After week 5, all the three groups showed an increase in pain (Fig. 1A). Similar patterns were seen when average IP pain and CMC pain were examined over 6 weeks (Fig. 1B and C).

4. Discussion

Our study identified three main patterns of hand pain (IP only, CMC only, and CMC and IP) in a community-based population participating in a clinical trial, with significant hand pain (VAS ≥ 40 out of 100 mm in any of the hand joints) and radiographic hand OA. Participants with pain in both the CMC and IP joints was most common and associated with higher pain, worse function and higher neuropathic-like pain compared to those with the CMC only or the IP only pain. All three groups had a significant reduction in pain and improvement in function over 6 weeks, with no significant difference among these three groups.

There is little information regarding on the natural history of pain according to the patterns of hand symptoms in hand OA. Our study

identified three different patterns of hand pain, with participants with both the CMC and IP pain showing more severe clinical symptoms compared to the other two groups. Previous data on hand pain phenotypes were cross-sectional and restricted to selective populations (Table 4) [13,14]. As with our study, Bijsterbosch et al. showed that those with both the CMC and IP pain had worst clinical outcomes [13]. Our study did not find a difference between the CMC only and the IP only groups for any clinical symptoms, which was similar to the study by Spacek et al. [14]. In contrast, the study by Bijsterbosch et al. reported significant difference between these two groups for AUSCAN pain and function [13]. The difference in findings among studies may be explained by the different definition of groups, different scaling of AUSCAN, different number of joints examined and number of participants in each group.

We found that symptoms tended to improve over 6 weeks, with no difference between those with both the CMC and IP pain and those with the CMC or the IP pain only. Although no previous study has examined the differences across hand pain groups, this is consistent with previously

Table 4
Description and results of the comparison studies.

Study	Population	Study designs	Demography	Outcomes	results
Current study	-People from community participating in an RCT (n = 99) - Selection criteria: ≥ 40 on a 100 mm VAS and KL grade ≥ 2 in at least one joint	-Longitudinal -Grouped based on the location of the significant pain ≥ 40 in VAS Group 1 = CMC only (n = 16), Group 2 IP only (n = 28), and Group 3 IP and CMC (n = 55) -Weekly data collected for 6 weeks -Joint included 4 DIP, 4 PIP, 1st IP in thumb, and 1 CMC	Age: 64.2 (7.4) Female: 91 (85.8%) BMI: 26.8 (4.1)	Pain: VAS AUSCAN (0–500) Function AUSCAN (0–900) Stiffness, Neuropathic-like pain	Baseline Data: - general hand pain, VAS Group 1 vs group 3: mean (SE) 51.2 (4.7) vs 68.1 (2.6); S Group 2 vs group 3: mean (SE) 59.3 (3.5) vs 68.1 (2.6); NS - general hand pain, AUSCAN Group 1 vs group 3: mean (SE) 237.9 (28.4) vs (290.1 (15.7); NS Group 2 vs group 3: mean (SE) 225.3 (21.2) vs 290.1 (15.7); S -Function, AUSCAN Group 1 vs group 3: mean (SE) 433.3 (55.7) vs 527.5 (30.9); NS Group 2 vs group 3: mean (SE) 356.0 (41.7) vs 527.5 (30.9); S Change in score: No difference Baseline Data: Group 2 and group 3: Pain Mean (SD) 6.1 (4.1) vs 8.9 (4.2): S Function Mean (SD) 10.6 (8) vs 15.6 (8.5): S (similar to current study) Group 1 vs group 3: Pain Mean (SD) 7.8 (3.9) vs 8.9 (4.2): NS (similar to current study) Function Mean (SD) 13.9 (8) vs 15.6 (8.5) Group 1 vs group 2: Pain mean (SD) 7.8 (3.9) vs 6.1 (4.1): NS (similar to current study) Function Mean (SD) 13.9 (8) vs 10.6 (8); NS
Bijsterbosch et al. [13]	-People from clinic (specialists or GP) participating in a study examining familial generalised OA or had hand OA at middle age (n = 308) -OA at multiple sites in addition to hand OA - Selection criteria: ACR or KL ≥ 2 or pain and stiffness on most days in addition to multiple bony swellings in the selected joints	-Cross-sectional -Grouped based on the location of symptoms (pain/stiffness) Group 1 = CMC Joint symptoms only (n = 20), Group 2 = IP Joint symptoms only (n = 138) and Group 3 = symptoms at both sites (n = 150). -Joint included 2 DIP, 2 PIP and 1 CMC	Age: 60.1 (7.3) Women: 86.4 BMI: 26.9 (4.6)	Pain: AUSCAN (0–20) Function AUSCAN (0–36)	Baseline Data: Group 2 and group 3: Pain Mean (SD) 6.1 (4.1) vs 8.9 (4.2): S Function Mean (SD) 10.6 (8) vs 15.6 (8.5): S (similar to current study) Group 1 vs group 3: Pain Mean (SD) 7.8 (3.9) vs 8.9 (4.2): NS (similar to current study) Function Mean (SD) 13.9 (8) vs 15.6 (8.5) Group 1 vs group 2: Pain mean (SD) 7.8 (3.9) vs 6.1 (4.1): NS (similar to current study) Function Mean (SD) 13.9 (8) vs 10.6 (8); NS
Spacek et al. [14]	-People from outpatients and inpatients from Physical Medicine and Rehabilitation and Rheumatology departments (n = 116) - Selection criteria: -ACR criteria	-Cross-sectional -Grouped based on patients' choice for the more severe pain and perceived disability (defined as the more bothersome location for activities of daily living). -Group with the base of the thumb, BT) (n = 67) and group with IP joints (n = 49) -joint included 2–5 IP and thumb	Age: 62.1 (7.4) Female 92.2% BM: not reported	VAS, (global pain, pain at base, pain in another digit) Cochin disability index Ritchie articular index: tenderness; Kapandji index; Grip strength; Perceived handicap	Baseline Data: - Group BT and group IP: global VAS right hand: mean (SD) 35.9 (29.8) vs 34.5 (27.4), NS Left hand: mean (SD) 29.5 (28.4) vs 34.2 (25.9); NS Functional disability: Mean (SD) 16.8 (12.6) vs 14. (14.1); NS (similar to current study)

Visual Analogue Scale, VAS; Australian Canadian Osteoarthritis Hand Index, AUSCAN; Functional Index for Hand OA, FIHOA; Carpometacarpal joint, CMC; Interphalangeal, IP; Significant, Base of the thumb, BT; American College of Rheumatology; ACR, mean (standard error), mean (SE); mean (standard deviation) 0, mean (SD); Significant, S; Non-significant, NS.

described improvement in hand pain over time [15].

The findings of this study add to knowledge about the characteristics and natural history of three common hand pain phenotypes (both CMC and IP, CMC only and IP only). Although the demographics of these three groups were similar, those with both the CMC and IP pain had higher clinical burden at baseline, with a trend for worse prognosis of hand pain and function over 6 weeks compared with those with the CMC pain only or the IP pain only. This may in part be explained by the greater number of joints involved, the longer duration of the disease, and presence of higher neuropathic-like pain in those with both the CMC and IP pain. The potential effect of neuropathic-like pain is supported by our findings of a lower prevalence of moderate to severe radiological OA (KL grade 3–4) and higher neuropathic-like pain in participants with both the CMC and IP pain, which is similar to previous findings [10,23].

Additionally, our results suggest that neuropathic-like pain may be especially important in those with pain at more than one site, irrespective of the degree of joint damage which is supported by previous data [24, 25]. The presence of neuropathic-like pain may reduce the efficacy of other therapies in OA [23]. This needs to be considered when developing treatment strategies for patients and consideration should be given to target neuropathic-like pain when present. As different hand pain phenotypes behave differently, the presence of both the CMC and IP pain may reduce the effect of interventions compared to the IP only or CMC only, especially if high levels of neuropathic-like pain are present. Identification of these different hand pain phenotypes has implications for clinical care and need to be considered in selection of subjects for clinical trials of hand OA.

A limitation of the current study is that we examined participants included in a clinical trial of topical corticosteroids for hand OA. The majority were recruited from the community with self-referral following advertisements through local and social media with minimal exclusions. Thus, our study findings are generalizable to community-based people with symptomatic and radiographic hand OA seeking management for their hand OA. We did not evaluate the erosive OA subtype due to the limited numbers, which needs further exploration. This study has some strengths. This is the first study to describe the natural history of pain and function in different hand pain phenotypes. We also examined weekly pain as recommended in the OARSI Clinical Trials Recommendations [8] and assessed total burden of hand pain over 6 weeks in those three groups. It is unclear why the pain level fluctuates weekly over time and understanding the significance of these patterns needs further investigations.

5. Conclusion

In community-based individuals with significant hand pain and radiographic hand OA, pain in both CMC and IP joints was more common than IP only and CMC only pain and identified as a more severe phenotype with higher levels of pain, reduced function, and increased neuropathic-like pain. However, changes in symptoms and function over 6 weeks were similar across the three groups. These data have the potential to inform clinical management of patients with hand pain, specially the importance of targeting neuropathic-like pain in patients with both the CMC and IP pain, and patient selection in clinical trials.

Funding

Mahnuma M Estee is a recipient of Bangabandhu Science and technology Fellowship from Ministry of Science and Technology, Government of the People's Republic of Bangladesh for her PhD. Yuan Z Lim is the recipient of NHMRC Clinical Postgraduate Scholarship (APP1133903) and Royal Australasian College of Physicians Woolcock Scholarship. Anita E Wluka is the recipient of the Royal Australian College of Physicians Fellows Career Development Fellowship. Flavia M Cicuttini is the recipient of National Health and Medical Research Council (NHMRC) Investigator Grant (APP1194829). The funding bodies had no role in the study design and conduct of the study; collection, analysis and interpretation of

the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Authors' contributions

Mahnuma M Estee: acquisition of data, analysis and interpretation of data, drafting the article and approval of the final manuscript. YuanYuan Wang: acquisition of data, analysis and interpretation of data, revising the draft critically and approval of the final manuscript. Yuan Z Lim: acquisition of data, revising the draft critically and approval of the final manuscript. Anita E Wluka: acquisition of data, revising the draft critically and approval of the final manuscript. Flavia M Cicuttini: conception and design of the study, analysis and interpretation of data, revising the draft critically and approval of the final manuscript. Flavia M. Cicuttini had full access to all the data in the study, took responsibility for the integrity of the data and the accuracy of the data analysis, and had final responsibility for the decision to submit for publication.

Declaration of competing interest

None.

Acknowledgements

Not applicable.

References

- [1] M. Michon, E. Maheu, F. Berenbaum, Assessing health-related quality of life in hand osteoarthritis: a literature review, *Ann. Rheum. Dis.* 70 (6) (2011) 921–928.
- [2] J. Wan, X. Qian, Z. He, Z. Zhu, P. Cheng, A. Chen, Epidemiological trends of hand osteoarthritis from 1990 to 2019: estimates from the 2019 global burden of disease study, *Front. Med.* 9 (2022).
- [3] I.N. Ackerman, R. Buchbinder, L. March, Global Burden of Disease Study 2019: an opportunity to understand the growing prevalence and impact of hip, knee, hand and other osteoarthritis in Australia, *Intern. Med. J.* 53 (10) (2023) 1875–1882.
- [4] M. Kloppenburg, W.Y. Kwok, Hand osteoarthritis—a heterogeneous disorder, *Nat. Rev. Rheumatol.* 8 (1) (2011) 22–31.
- [5] M. Kloppenburg, F.P.B. Kroon, F.J. Blanco, M. Doherty, K.S. Dziedzic, E. Greibrokk, et al., 2018 update of the EULAR recommendations for the management of hand osteoarthritis, *Ann. Rheum. Dis.* 78 (1) (2019) 16.
- [6] W. Zhang, M. Doherty, B.F. Leeb, L. Alekseeva, N.K. Arden, J.W. Bijlsma, et al., EULAR evidence based recommendations for the management of hand osteoarthritis: report of a task force of the EULAR standing committee for international clinical studies including therapeutics (ESCSIT), *Ann. Rheum. Dis.* 66 (3) (2007) 377–388.
- [7] R. Altman, G. Alarcon, D. Appelrouth, D. Bloch, D. Borenstein, K. Brandt, et al., The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand, *Arthritis Rheum.* 33 (11) (1990) 1601–1610.
- [8] M. Kloppenburg, E. Maheu, V.B. Kraus, F. Cicuttini, M. Doherty, R.L. Dreiser, et al., OARSI Clinical Trials Recommendations: design and conduct of clinical trials for hand osteoarthritis, *Osteoarthritis Cartilage* 23 (5) (2015) 772–786.
- [9] S. van Beest, L.A. van de Stadt, F.R. Rosendaal, M. Kloppenburg, Patients with clinically diagnosed hand OA not fulfilling the ACR classification criteria are in an earlier disease phase and more often have thumb base OA, *Osteoarthritis and Cartilage Open* 5 (2) (2023) 100347.
- [10] M. Marshall, D. van der Windt, E. Nicholls, H. Myers, E. Hay, K. Dziedzic, Radiographic hand osteoarthritis: patterns and associations with hand pain and function in a community-dwelling sample, *Osteoarthritis Cartilage* 17 (11) (2009) 1440–1447.
- [11] I.K. Haugen, P. Bøyesen, Imaging modalities in hand osteoarthritis—and perspectives of conventional radiography, magnetic resonance imaging, and ultrasonography, *Arthritis Res. Ther.* 13 (6) (2011) 248.
- [12] M. Marshall, H. Jonsson, G.P. Helgadottir, E. Nicholls, D. van der Windt, H. Myers, et al., Reliability of assessing hand osteoarthritis on digital photographs and associations with radiographic and clinical findings, *Arthritis Care Res.* 66 (6) (2014) 828–836.
- [13] J. Bijsterbosch, W. Visser, H.M. Kroon, T. Stamm, I. Meulenbelt, T.W. Huizinga, et al., Thumb base involvement in symptomatic hand osteoarthritis is associated with more pain and functional disability, *Ann. Rheum. Dis.* 69 (3) (2010) 585–587.
- [14] E. Spacek, S. Poiraudou, F. Fayad, M.M. Lefevre-Colau, J. Beaudreuil, F. Rannou, et al., Disability induced by hand osteoarthritis: are patients with more symptoms at digits 2-5 interphalangeal joints different from those with more symptoms at the base of the thumb? *Osteoarthritis Cartilage* 12 (5) (2004) 366–373.
- [15] Y. Wang, M.M. Estee, D. Gan, Y.Z. Lim, S. Heritier, A.E. Wluka, et al., Effect of 6-week treatment with topical betamethasone dipropionate in patients with symptomatic hand osteoarthritis: a randomized double-blind, placebo-controlled trial, *Osteoarthritis and Cartilage Open* 5 (3) (2023) 100382.

- [16] J.H. Kellgren, J.S. Lawrence, Radiological assessment of osteo-arthrosis, *Ann. Rheum. Dis.* 16 (4) (1957) 494–502.
- [17] Y. Wang, S.M. Hussain, D. Gan, Y.Z. Lim, M.M. Estee, S. Heritier, et al., Topical corticosteroid for treatment of hand osteoarthritis: study protocol for a randomised controlled trial, *BMC Musculoskel. Disord.* 22 (1) (2021) 1036.
- [18] A.W. Visser, P. Boyesen, I.K. Haugen, J.W. Schoones, D.M. van der Heijde, F.R. Rosendaal, et al., Instruments measuring pain, physical function, or patient's global assessment in hand osteoarthritis: a systematic literature search, *J. Rheumatol.* 42 (11) (2015) 2118–2134.
- [19] N. Bellamy, J. Campbell, B. Haraoui, E. Gerez-Simon, R. Buchbinder, K. Hobby, et al., Clinimetric properties of the AUSCAN Osteoarthritis Hand Index: an evaluation of reliability, validity and responsiveness, *Osteoarthritis and cartilage/OARS, Osteoarthritis Research Society* 10 (11) (2002) 863–869.
- [20] R.L. Dreiser, E. Maheu, G.B. Guillou, H. Caspard, J.M. Grouin, Validation of an algofunctional index for osteoarthritis of the hand, *Revue du rhumatisme (English ed)* 62 (6 Suppl 1) (1995) 43s–53s.
- [21] R. Freynhagen, R. Baron, U. Gockel, T.R. Tölle, Pain DETECT: a new screening questionnaire to identify neuropathic components in patients with back pain, *Curr. Med. Res. Opin.* 22 (10) (2006) 1911–1920.
- [22] R.D. Altman, G.E. Gold, Atlas of individual radiographic features in osteoarthritis, revised, *Osteoarthritis Cartilage* 15 (Suppl A) (2007) A1–A56.
- [23] C. van der Meulen, L.A. van de Stadt, F.P.B. Kroon, M.C. Kortekaas, A. Boonen, S. Böhringer, et al., Neuropathic-like pain symptoms in inflammatory hand osteoarthritis lower quality of life and may not decrease under prednisolone treatment, *Eur. J. Pain* 26 (8) (2022) 1691–1701.
- [24] P. Steen Pettersen, T. Neogi, K. Magnusson, A. Mathiessen, H.B. Hammer, T. Uhlig, et al., Associations between joint pathologies and central sensitization in persons with hand osteoarthritis: results from the Nor-Hand study, *Rheumatology* 61 (6) (2022) 2316–2324.
- [25] S. Thapa, R.H. Shmerling, J.F. Bean, Y. Cai, S.G. Leveille, Chronic multisite pain: evaluation of a new geriatric syndrome, *Aging Clin. Exp. Res.* 31 (8) (2019) 1129–1137.