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TITLE: **HAND EXAMINATION, ULTRASOUND AND ITS ASSOCIATION WITH HAND PAIN AND FUNCTION IN COMMUNITY-BASED OLDER ADULTS.**

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Competing interest statement

The authors declare no competing interest.

Abstract

Objective: To describe cross-sectional associations between features observed on ultrasound (US) or clinical joint examination and hand symptoms amongst community-dwelling older adults (n=519), and determine whether such associations are independent of age, sex, BMI, and other imaging features.

Methods: Hand pain, function, and stiffness were assessed using a visual analogue scale (VAS) and the Australian/Canadian hand osteoarthritis (AUSCAN) index. Standardised clinical and ultrasound examinations were performed. Grip strength was assessed using dynamometer. Data were analysed using hurdle and linear models and adjusted for demographic factors and other features.

Results: Abnormal findings on joint examination and visualised by ultrasound are common in older adults with and without hand pain. Greater numbers of tender joints were associated with greater pain (VAS, β=2.63 (95% CI; 1.88, 3.39)); AUSCAN pain, β=10.57 (4.00, 17.13)), poorer AUSCAN function (β=4.07 (1.28, 6.86)), and poorer grip strength (β=-0.15 psi (-0.27, -0.03)). Power Doppler imaging (PDI) synovitis was associated with greater pain (VAS β=2.61 (1.03, 4.19), AUSCAN pain (β=13.07 (3.82, 22.32)), but not function. Joint deformity was associated with poorer function (β=4.51 (1.75, 7.26)) and grip strength (β=-0.23 (-0.40, -0.05)) but not pain. Grey-scale synovitis was associated only with poorer grip strength (β=-0.22 (-0.41, -0.04)). Associations with function and grip strength were partially mediated by pain.

Conclusion: Joints which are tender on palpation or have US-identified PDI synovitis are potential treatment targets for hand pain. Treating tender joints and preventing hand deformity is required to improve hand function in community-dwelling older adults.

Keywords: hand osteoarthritis, ultrasound, clinical hand assessment, physical hand assessment, hand pain, hand function, stiffness.

Significance and Innovation

- This is the first study to report prevalence and severity of ultrasound-detected hand abnormalities in community-dwelling older adults.
- This study adds to existing evidence that inflammation assessment using ultrasound adds greater importance to assess hand abnormalities than clinical hand assessment alone.

Introduction

Hand pain is common in older adults (1, 2), and is associated with poorer hand function (3), and difficulty performing everyday tasks (4, 5). Both clinical examination and imaging are routinely used to assess hand pain. However, radiography is the usual imaging method, yet radiographic changes are weakly associated with pain and function (3, 6-8). Ultrasonography is a promising technique for imaging hand joints as it assesses surface joints clearly and quickly, is often available in consultation rooms, and involves no radiation exposure, but assessments of whether abnormal joints seen on ultrasound (US) are associated with pain and symptoms are needed (9).

Previous studies which used ultrasound to image hand joints have shown that osteophytes were associated with pain (10), but associations between synovitis and pain are inconsistent in hand osteoarthritis (OA) patients (10-12). Sum of scores of grey-scale synovitis (a composite of synovial hypertrophy and effusion) was independently associated with Australian/Canadian hand osteoarthritis (AUSCAN) pain in one study (10). Associations between Power Doppler Imaging (PDI) synovitis and pain are inconsistent either at joint or patient level, with PDI synovitis associated with palpated pain in some studies (10, 13), but not others at joint (11) and patient level (12). All of these studies had small numbers of participants (25 to 55 participants) (10-14), and all were in patients with hand OA. Association between grey-scale synovitis and pain are independent of other ultrasound features (10), but whether PDI synovitis is also independent of other ultrasound features is unknown (13). Similarly, no studies have assessed whether associations between ultrasound features and physical function are independent of pain.

Only two studies have assessed associations between abnormal hand features on US and physical function limitation. One study showed that sum of score of grey-scale synovitis was associated with worse Short-Form-36 (SF-36) physical component summary score (10); however, another study found no association between sum of score of PDI synovitis, grey-scale synovitis, or osteophytes with AUSCAN function limitation (12).

Therefore, we aimed to describe cross sectional associations between clinically evident swelling, tenderness, nodules, deformity, and ultrasound-detected osteophytes, grey-scale synovitis, and PDI synovitis with hand pain, stiffness, physical function limitation, and grip strength in a community dwelling cohort of older adults. This will enable us to assess whether associations are independent of age, sex and other factors, and whether US findings add value to clinical assessment.

Methods

Participants

The Tasmanian older adult cohort (TASOAC) study is a prospective, population-based study which aimed to identify environmental, genetic, and biochemical factors associated with development and progression of OA at multiple sites (hand, knee, hip, and spine). Participants aged 50-80 years (n=1099) were recruited from the electoral roll in Southern Tasmania in 2002 using sex stratified random sampling (response rate 57%). Participants were excluded if they were institutionalised or reported contraindications to MRI. Data on hand osteoarthritis (OA) features were collected only at the 10-year follow-up (Phase 4, n=519); therefore, analyses in this manuscript consisted of cross-sectional data from Phase 4.

All research conducted was in compliance with the Declaration of Helsinki and was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee. All subjects gave informed written consent.

Outcomes: Hand pain, stiffness, physical function limitation

Pain in target hand: Visual analogue scale

Study participants were asked to assess pain in their target hand "on this line, where would you rate your pain? Use the last seven days as a time frame". This was assessed using a single item question of generic pain on 100mm visual analogue scale (VAS), a valid (15, 16) and reliable (16) measure of hand pain in rheumatic conditions. The target hand was the participant's dominant hand unless they had contraindications to either magnetic resonance imaging (MRI) or high resolution peripheral quantitative CT (HRpQCT), in which case the contralateral hand was examined instead. This paper utilises only the ultrasound data.

Pain in both hands: AUSCAN Osteoarthritis Hand Index VA3.1

Hand pain, stiffness and difficulty performing daily activities in both hands was assessed using the Australian/Canadian hand osteoarthritis (AUSCAN) index questionnaire VA3.1, which is a valid, reliable, and responsive measure for hand OA (17). The time horizon was the last 48 hours and questions were assessed using a 100mm VAS. AUSCAN consists of a total of 15 questions (5 for pain, 1 for (morning) stiffness, and 9 for physical function).

Clinical examination

Bilateral clinical joint examination of all 15 joints in each hand were performed by one trained assessor (CB). Presence or absence of tenderness, soft tissue swelling, hard tissue enlargement (nodules) and deformity were assessed based on American College of Rheumatology (ACR) criteria for hand OA (18). Briefly, tenderness was assessed by the examiner exerting sufficient pressure on each joint using their thumb and index finger to produce whitening of the examiners nail bed (19). Swollen joints were assessed visually and by palpation. Finger nodules were assessed by manual examination of each joint and deformity was determined by the appearance of any deviation in the joint from the sagittal plane. Joint pain in the target hand was also determined by asking participants if they had pain (yes/no) in each individual joint in the preceding seven days. Information from the clinical hand examination was used to diagnose clinically defined hand OA using ACR criteria (18). The intra-observer reliability of each abnormalities at joint level was assessed with at least a one-week interval between the readings using kappa-statistic (20) in 10 participants. The results were fair to substantial; k=0.376 (95% CI 0.061,0.690) for left hand deformity, k=0.495 (0.211, 0.779) for left hand tenderness, k=0.606 (0.467, 0.746) for left hand nodules, k=0.668 (0.537, 0.799) for right hand nodules, and k=0.688 (0.431, 0.946) for right hand deformity. Swollen and tender joints in the right hand, and swollen joints in the left hand had too little variability to enable kappa to be calculated.

Ultrasound assessment

Ultrasound assessments were completed by one experienced ultrasonographer (KS) using a GE LOCIQ *e* (GE Medical Systems (China) Co. LTD Jiangsu, P.R. China) and a L8-18i hockey stick transducer using the methods of Keen et al. (12). Power Doppler was assessed utilising a pulse repetition frequency (PRF) of

0.8kHz and medium wall filter (138Hz) (21). Gain was adjusted until the background signal was eliminated. Each patient's target hand was examined with the patient seated at the scanning table.

Fifteen joints of the hand were assessed: the 1st carpometacarpal joint, 1st to 5th metacarpophalangeal joints, 1st to 5th proximal interphalangeal joints and 2nd to 5th distal interphalangeal joints. Following established protocols, the dorsal aspects of each joint was assessed by ultrasound for osteophytes, grey-scale synovitis, and PDI synovitis (22). Each joint was scanned in the longitudinal and transverse planes.

Imaging features were scored on a semi quantitative 0-3 scale for each joint. Osteophytes were defined as cortical protrusions seen in both the longitudinal and transverse planes, grey-scale synovitis was defined as a composite of both effusion and synovial hypertrophy, and PDI synovitis was defined as power Doppler signal identified within the synovium of the area of grey-scale synovitis (22). For each of the grey-scale synovitis and osteophytes, joints were classified as follows: 0 = no pathology, 1 = mild pathology, 2 = moderate pathology, 3 = severe pathology (21, 22). Similarly, PDI synovitis was scored as 0 = no PDI signal within the synovium adjacent to the joint, 1 = minimal PDI signal, 2 = moderate signal, 3 = marked evidence of PDI signal (22). Intra-rater reliability for ultrasound measures at joint level was determined by reimaging a subgroup of 20 participants on the same day as their original assessment. Reliability was assessed using weighted kappa. Reliability for all measures was substantial $k_{(w)} = 0.753$ (CI; 0.730 to 0.760) for osteophytes, $k_{(w)} = 0.661$ (0.586 to 0.719) for grey-scale synovitis, $k_{(w)} = 0.689$ (0.525 to 0.780) for PDI synovitis.

All of the participants had at least 1 joint with osteophyte and grey-scale synovitis, therefore, we collapsed categories for analysis, dichotomising osteophytes and grey-scale synovitis as ≥ 2 (due to the high prevalence) and PDI synovitis score ≥ 1 measured on ultrasound as present or absent on each of the 15 joints, and summed the number of joints with abnormalities.

Other factors

BMI was calculated as weight (kg)/height $(m)^2$ using weight measured to the nearest 0.1kg using a single set of calibrated electronic scales (Seca Delta Model 707), and ^{height} measured to the nearest 0.1cm using a stadiometer, minus shoes, socks and headwear. Grip strength was measured by North Coast™ Bulb Dynamometer; adult 0-30 psi, model no. 70154 with the participant sitting with the shoulder in a neutral

position and 90-degree flexed elbow. The best performance out of two attempts was recorded for each hand. In this study, we used measurements of the target hand. Any pain medication used were recorded in self-reported questionnaire from the list of medications they were taking (medication name, dose and frequency).

Statistical analyses

The primary exposure for all analyses was number of joints with features on clinical assessment (tenderness, swollen, nodules, and deformity; both hands for AUSCAN scales and target hand only for association with target hand VAS pain score and grip strength) and ultrasound assessment (osteophytes, grey-scale synovitis, and PDI synovitis).

We used exponential hurdle models to estimate associations between number of joints with clinical and ultrasound features and the outcomes; target hand VAS pain score, AUSCAN subscales and total AUSCAN scores are bounded by zero and non-normally distributed with a large number of zeros. The distribution of the outcomes (bimodal, given the large number of people with no pain) meant that the data is difficult to model and simpler methods e.g. linear regression were not suitable. The hurdle models had two components: presence and absence of pain and pain severity, which were modelled separately. Model coefficients estimate the average marginal effects (predicted changes in pain) for a one unit increase in number of joints with abnormalities (Table 2 and 3). Linear regression was used to assess association between target hand grip strength. To assess independence of associations, all models were adjusted for age, sex and body mass index (BMI) and further adjusted for pain (for function limitation and grip strength), and then all other clinical or ultrasound variables.

We conducted sensitivity analysis to examine whether pain medication use was a confounder. All statistical analyses were performed using Stata 15 SE (Stata-Corp, College Station, Texas, USA). P-values ≤0.05 (two-tailed) were considered statistically significant.

Results

Study participants

Included participants attended the 10 year TASOAC follow up, a subset of the original cohort. They were younger at baseline (mean (SD); 61.4 (6.6) vs 64.0 (7.9) years; p-value<0.001, n=519) and had greater steps per day (9150 (3314) vs 8115 (3318) steps/day; p-value<0.001) than those who were lost to follow up. There was a similar proportion of women (49% vs 53%; p-value=0.30), average BMI (27.6 (4.4) vs 28.2 (5.0) kg/m^2; p-val=0.05), and proportion of current smokers (11% vs 13%;p-value=0.18) compared to those who were lost to follow-up.

Table 1 shows the characteristics of study participants stratified by presence or absence of hand pain, assessed by AUSCAN pain score. Participants with hand pain were of similar age and BMI to those with no pain, but more female, a higher proportion of them met ACR hand OA criteria, and had clinical and ultrasound features (except where features were ubiquitous (i.e. nodules)). All of the participants had score of at least 1 for osteophytes and grey-scale synovitis, therefore we dichotomised them (above / below 2, at the joint level), thus 92% of joints had osteophytes, 41% had grey-scale synovitis, and 3.5% had PDI synovitis (Table 1).

Hand pain

Greater numbers of clinically swollen, tender, deformed joints, and joints with ultrasound-detected osteophytes, grey-scale synovitis or PDI synovitis were associated with more intense pain in the target hand (Table 2) and AUSCAN pain score (Table 3), after adjustment for age, sex, and BMI. However, these associations persisted only for target hand's number of tender joints and PDI synovitis after further adjustment for other clinical or ultrasound features (Table 2, Table 3).

Number of joints with nodules was not associated with either VAS or AUSCAN hand pain (Table 2, 3).

Hand physical function limitation

Greater numbers of clinically swollen, tender or deformed joints and ultrasound-detected osteophytes, grey-scale synovitis, and PDI synovitis were all associated with increased function limitation scores after adjustment for age, sex and BMI (Table 3). After further adjustment for AUSCAN pain score, effect sizes reduced and remained statistically significant only for number of tender and deformed joints; these reduced slightly after further adjustment for all other clinical assessment features, but remained statistically significant.

Number of clinically swollen and nodulous joints, ultrasound-detected osteophytes, grey-scale synovitis, and PDI synovitis were not associated with function limitation scores after adjustment of AUSCAN pain score and all other ultrasound features (Table 3).

Hand stiffness

Number of joints with clinically swollen, tender, nodules, deformity and ultrasound-detected osteophytes, grey-scale synovitis, and PDI synovitis were associated with greater stiffness score, after adjustment for demographic factors (Table 3). After further adjustment for AUSCAN pain score, associations remained statistically significant for number of joints with tenderness, nodules, and osteophytes. These associations only persisted for nodules and osteophytes after adjustment for other clinical or ultrasound features.

Total AUSCAN score

Greater numbers of joints with swollen, tender, deformed joints, osteophytes, grey-scale synovitis or PDI synovitis were associated with greater total AUSCAN score, after adjustment for demographic factors (Supplementary Table 1). Associations remained significant for number of joints with tenderness, deformity, and PDI synovitis after further adjustment for other clinical or ultrasound features.

222

223 ***Hand grip strength***

224

225 Greater numbers of joints with tenderness, nodules, deformities on target hand, and abnormalities in all
226 ultrasound features were associated with weaker grip strength for all abnormal features after adjustment
227 for age, sex, and BMI (Table 4). Excepting associations with PDI synovitis, effect sizes reduced slightly after
228 further adjustment for AUSCAN pain, but remained statistically significant. Associations between tender
229 and deformed joints and joints with grey-scale synovitis remained statistically significant after further
230 adjustment for other clinical or ultrasound features with only small reductions in effect size. (Table 4).

231 We further adjusted all our models for any use of pain medication. This did not change the effect sizes by
232 more than 10% (data not shown).

Discussion

This study is the first to report prevalence and severity of ultrasound-detected hand osteoarthritis abnormalities in community-dwelling older adults. Greater number of joints which were tender on palpation or had PDI synovitis on US were associated with hand pain independent of other findings on clinical examination or US. Greater number of joints which were tender or deformed on clinical examination; or with grey-scale synovitis on US were associated with function limitation or lower grip strength. Associations between these abnormalities and function limitation, grip strength, and stiffness were predominantly mediated through pain; however, tenderness and deformity affected function even after taking pain into account.

Prevalence estimates for abnormal imaging features were similar to those reported in cohorts of people with hand OA: 41% of joints had grey-scale synovitis, compared to 25% to 46% in other studies (10, 12, 13); similarly 3.5% of joints had PDI synovitis, compared to literature estimates of 2% to 9% (10, 12, 23-25). However, prevalence of ultrasound-detected osteophytes in our study was higher than literature estimates (range 41% to 85%) (14, 26, 27), this may be explained by differences in average ages of the cohort (ours is >10 years older). We expected the abnormalities prevalence to be smaller than estimates from hand OA cohorts, however, our study suggests that these abnormalities are common in the general population of older people.

These results suggest that the most important aspect of the clinical examination is identifying people with tender joints on palpation, a specific type of pain present in only a small proportion (7%) of people with hand pain, and with joint deformity. The former is important for both pain and function, the latter only for function. Similarly, the most important US finding is PDI synovitis.

Associations between tender joints and PDI synovitis with hand pain (both pain in the target hand and AUSCAN pain) are in contrast to two studies which found no associations between number of joints with ultrasound features and hand pain (12, 28). However, both of these studies were likely underpowered to detect an association due to a small number of participants in these studies (<20 participants). This

suggests that our findings are real associations, and that the negative finding in the literature may be false negatives.

Associations between greater number of tender and deformed joints (but not nodules) and physical function limitation (assessed by AUSCAN function and grip strength) is consistent with two previous studies (28, 29), although we are the first to demonstrate that these associations are independent of other clinical features, as well as partially mediated by pain. Meanwhile, the latter differs from other studies, where Jones et al. and Bagis et al. reported that Heberden's nodes were associated with physical function (but were not independent of pain) (3, 29). This suggests that improving joint tenderness may improve hand function, and that preventing deformity may also improve hand function.

Associations between greater number of joints with nodules and osteophytes and greater AUSCAN stiffness score in our study are consistent with a cross sectional study of 190 women with hand OA (30), but not a case control study of 55 adults with and without hand OA (12), although the reason for the different findings is unclear. Kortekaas et al. showed weak associations between grey-scale synovitis and stiffness, however they did not adjust for pain or other ultrasound features (10). In our study, associations between grey-scale synovitis and stiffness were not independent of pain or other features. This suggests that improving hand stiffness will require improvements in hand pain.

We demonstrated that ultrasound-detected PDI synovitis signal was independently correlated with pain, while combined synovial hypertrophy and effusion (grey-scale synovitis) was not. Therefore, successfully treating PDI synovitis may improve hand pain, but treating grey-scale synovitis may not. Additionally, since PDI synovitis is associated with radiographic damage and reduced cartilage thickness in hand OA at joint level cross-sectionally (11, 24, 31); our results support PDI synovitis as an important correlate of structural abnormalities in hand pain and thereby represent a treatment target for reducing hand pain and progression of hand OA.

Strengths of this study include the standardised clinical assessment and ultrasound data, conducted by a single experienced assessor; and the population-based source of the data; which enables findings to be generalised to older adults in the community.

Limitations include loss to follow up within the TASOAC cohort: data used for this study is a subset of the original cohort (with 53% lost to follow up over 10.7 years); however, the cohort retained is largely representative of the original cohort. Therefore, the risk of bias from participants lost to follow up is low and the results remain generalisable to older people. While the generalisable cohort is a strength, it also means that the study includes people with other rheumatic conditions common in older adults, meaning that abnormalities observed could be due to a range of underlying conditions. The ultrasound assessment scoring system does not include erosion assessment (12) because ultrasound is less sensitive to the presence of erosions than conventional radiography (32). Other limitations include a limited field of view for the ultrasound, with ultrasound examination performed on the dorsal side of each finger joint only. This is in line with established protocols within the field (12, 14). While it is possible that this might under-estimate prevalence of ultrasound abnormalities, this is unlikely as ultrasound abnormalities were extremely common. Additionally, the study is cross-sectional and therefore inferences regarding causality are limited.

Conclusion

Joints which are tender on palpation, and have PDI synovitis on ultrasound are independently associated with hand pain and are potential treatment targets for hand pain. Joints which are tender, deformed or have grey-scale synovitis are associated with reduced function or grip strength cross-sectionally. Associations with function were predominantly mediated through pain; however, tenderness and deformity remained associated with function even after adjusting for pain. Therefore, treating tender joints and preventing hand deformity is required to improve hand function in community-dwelling older adults.

Declarations

Ethics approval and consent to participate

All research conducted was in compliance with the Declaration of Helsinki and was approved by the Southern Tasmanian Health and Medical Human Research Ethics Committee. All subjects gave informed written consent.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author's contributions

All authors were involved in drafting the article or revising it for important intellectual content. All authors have approved the final manuscript. Graeme Jones (graeme.jones@utas.edu.au) takes responsibility for the integrity of the work as a whole, from inception to finished article.

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Table 1. Characteristics of study participants, by presence or absence of hand pain on AUSCAN.

	Whole sample (n=519)		No hand pain (AUSCAN pain=0) (n=210)		Hand pain (AUSCAN pain>0) (n=309)	
Age	72.05 (6.41)		72.11 (6.01)		72.01 (6.67)	
Female (%)	50		42		54	
BMI (kg/m^2)	28.03 (4.88)		27.91 (4.75)		28.11 (4.97)	
Met ACR HOA criteria (%)	67		41		84	
Grip strength	10.96 (3.77)		11.76 (3.45)		10.41 (3.88)	
	%	No. of joints (0-30)	%	No. of joints (0-30)	%	No. of joints (0-30)
Clinical assessment						
Swollen	48	0.1 (0.8)	22	0.1 (0.4)	65	0.2 (1.0)
Tenderness	5	2.0 (4.1)	2	0.4 (1.0)	7	3.1 (4.9)
Nodules	100	22.3 (7.3)	100	21.7 (6.8)	100	22.7 (7.6)
Deformity	66	2.1 (2.5)	60	1.7 (2.3)	70	2.3 (2.6)
	%	No. of joints (0-15)	%	No. of joints (0-15)	%	No. of joints (0-15)
Ultrasound features						
Osteophytes	97	5.93 (3.28)	96	5.38 (3.18)	97	6.29 (3.29)
Grey-scale synovitis	53	1.05 (1.41)	42	0.75 (1.17)	60	1.25 (1.51)

PDI synovitis	33	0.52 (0.96)	23	0.34 (0.72)	40	0.65 (1.08)

Mean (standard deviation) except for percentage.

Presence of osteophytes and grey-scale synovitis at joint level is dichotomised to ≥2, other clinical and ultrasound features were dichotomised at ≥1.

n, number; BMI, body mass index; VAS, visual analogue scale; AUSCAN, Australian/Canadian hand osteoarthritis index; no., number; ACR HOA, American College of Rheumatology criteria for hand osteoarthritis; PDI, power Doppler imaging.

Table 2. Associations between number of joints with target hand clinical and ultrasound features of osteoarthritis and target hand pain by VAS during the last 7 days.

	Target hand pain by VAS (mm)	
	Adjusted for age, sex, and BMI. β (95% CI)	Further adjusted for clinical/US features[†] β (95% CI)
No. of joints (clinical)		
Swollen	**7.73 (3.15, 12.32)**	3.55 (-0.04, 7.14)
Tender	**2.84 (2.07, 3.61)**	**2.63 (1.88, 3.39)**
Nodules	0.29 (-0.15, 0.73)	0.14 (-0.26, 0.54)
Deformity	**1.88 (0.70, 3.06)**	0.44 (-0.62, 1.49)
No. of joints (ultrasound)		
Osteophytes	**0.78 (0.23, 1.32)**	0.42 (-0.15, 1.00)
Grey-scale synovitis	**1.69 (0.62, 2.77)**	0.44 (-0.79, 1.66)
PDI synovitis	**3.17 (1.69, 4.64)**	**2.61 (1.03, 4.19)**

[†]further adjusted for other clinical features (for clinical exposures) or other ultrasound features (for ultrasound exposures).

Presence of osteophytes and grey-scale synovitis at joint level is dichotomised to ≥2, other clinical and ultrasound features were dichotomised at ≥1.

Associations were assessed using hurdle model.

VAS, visual analogue scale; US, ultrasound; PDI, power Doppler imaging; CI, confidence interval.

Bold denotes a statistically significant result.

Table 3. Associations of number of joints with clinical and ultrasound osteoarthritis features and AUSCAN scales.

	Pain score (mm)		Physical function limitation score (mm)			Stiffness score (mm)		
Adjusted for	age, sex, and BMI β (95% CI)	Further adjusted for clinical/US features[†] β (95% CI)	age, sex, and BMI β (95% CI)	Further adjusted for AUSCAN pain β (95% CI)	Further adjusted for clinical/US features[†] β (95% CI)	age, sex, and BMI β (95% CI)	Further adjusted for AUSCAN pain β (95% CI)	Further adjusted for clinical/US features[†] β (95% CI)
No. of joints (clinical)								
Swollen	**16.69 (5.55, 27.83)**	1.08 (-6.26, 8.42)	**35.53 (11.44, 59.63)**	7.97 (-1.27, 17.22)	6.26 (-3.18, 15.71)	**2.70 (0.66, 4.75)**	0.53 (-0.91, 1.97)	0.68 (-0.82, 2.19)
Tender	**10.95 (4.20, 17.69)**	**10.57 (4.00, 17.13)**	**25.97 (18.78, 33.15)**	**4.81 (1.97, 7.64)**	**4.07 (1.28, 6.86)**	**1.83 (1.35, 2.30)**	**0.37 (0.04, 0.71)**	0.31 (-0.02, 0.65)
Nodules	0.83 (-0.30, 1.96)	0.23 (-0.65, 1.10)	2.30 (-0.06, 4.67)	0.91 (-0.18, 2.01)	0.49 (-0.64, 1.61)	**0.38 (0.14, 0.62)**	**0.25 (0.07, 0.43)**	**0.27 (0.08, 0.46)**
Deformity	**6.64 (3.05, 10.24)**	2.13 (-0.15, 4.42)	**15.56 (7.92, 23.20)**	**5.41 (2.74, 8.08)**	**4.51 (1.75, 7.26)**	**1.29 (0.60, 1.97)**	0.25 (-0.14, 0.64)	0.06 (-0.46, 0.57)
No. of joints (ultrasound)								
Osteophytes	**3.96 (1.12, 6.80)**	2.64 (-0.45, 5.73)	**8.27 (2.44, 14.10)**	2.11 (-2.89, 7.12)	-0.38 (-6.11, 5.35)	**1.09 (0.52, 1.67)**	**0.53 (0.10, 0.96)**	**0.51 (0.03, 0.99)**
Grey-scale synovitis	**7.42 (1.67, 13.16)**	1.27 (-5.37, 7.92)	**21.46 (8.91, 34.01)**	11.23 (-0.02, 22.47)	9.94 (-3.08, 22.97)	**1.63 (0.50, 2.75)**	0.52 (-0.32, 1.35)	-0.20 (-1.19, 0.80)

PDI synovitis	**15.76 (7.22, 24.29)**	**13.07 (3.82, 22.32)**	**35.99 (17.5, 54.49)**	11.43 (-3.99, 26.86)	6.20 (-10.70, 23.10)	**3.49 (1.80, 5.18)**	1.15 (-0.08, 2.37)	0.92 (-0.42, 2.27)

Associations were assessed using hurdle model.

[†]further adjusted for other clinical features (for clinical exposures) or other ultrasound features (for ultrasound exposures).

Presence of osteophytes and grey-scale synovitis at joint level is dichotomised to ≥2, other clinical and ultrasound features were dichotomised at ≥1.

US, ultrasound; PDI, power Doppler imaging; CI, confidence interval.

Bold denotes a statistically significant result.

Table 4. Associations of number of joints with target hand clinical and ultrasound features and grip strength of target hand(psi).

	Grip strength (psi)		
	Adjusted for age, sex, and BMI. β (95% CI)	Further adjusted for AUSCAN pain β (95% CI)	Further adjusted for clinical/US features† β (95% CI)
No. of joints (clinical)			
Swollen	**-0.46 (-0.89, -0.03)**	-0.19 (-0.62, 0.23)	-0.10 (-0.53, 0.33)
Tender	**-0.32 (-0.42, -0.23)**	**-0.18 (-0.3, -0.07)**	**-0.15 (-0.27, -0.03)**
Nodules	**-0.09 (-0.16, -0.03)**	**-0.08 (-0.14, -0.02)**	-0.06 (-0.12, 0.005)
Deformity	**-0.40 (-0.58, -0.23)**	**-0.31 (-0.48, -0.14)**	**-0.23 (-0.40, -0.05)**
No. of joints (ultrasound)			
Osteophytes	**-0.14 (-0.20, -0.07)**	**-0.10 (-0.17, -0.04)**	-0.08 (-0.16, 0.004)
Grey-scale synovitis	**-0.33 (-0.47, -0.20)**	**-0.27 (-0.40, -0.13)**	**-0.22 (-0.41, -0.04)**
PDI synovitis	**-0.31 (-0.51, -0.11)**	-0.14 (-0.34, 0.06)	0.10 (-0.15, 0.347)

†further adjusted for other clinical features (for clinical exposures) or other ultrasound features (for ultrasound exposures).

Presence of osteophytes and grey-scale synovitis at joint level is dichotomised to ≥2, other clinical and ultrasound features were dichotomised at ≥1.

Associations were assessed using linear regression.

US, ultrasound; PDI, power Doppler imaging; CI, confidence interval.

Bold denotes a statistically significant result.