Erosive and osteoarthritic structural progression in early rheumatoid arthritis

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Abbreviations: RA – rheumatoid arthritis, DAS – disease activity score, JSN – joint space narrowing, HAQ – health assessment questionnaire, EULAR – European League Against Rheumatism, WHO-world health organisation, OA – osteoarthritis, OST – osteophyte, MTX-methotrexate, SSZ-sulphasalazine, DAS28 – 28 joint disease activity score, TJC-tender joint count, SJC-swollen joint count, VAS-visual analogue scale, GH- general health, ESR – erythrocyte sedimentation rate, HAQ-health assessment questionnaire, SF36 – 36 question short form questionnaire, ERAN – early rheumatoid arthritis network, ERAS – early rheumatoid arthritis study, MCP – metacarpal, CMC-

carpal-metacarpal, DIP-distal interphalangeal, PIP-proximal interphalangeal, MTP-metatarsophalangeal , CMT – cuneo metatarsal

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Abstract

Objectives

To investigate associations with joint damage in early Rheumatoid arthritis (RA), and how comorbid osteoarthritis (OA) might influence patient assessment and outcomes.

Methods

Baseline radiographs of hands/feet from 512 participants in the Early RA Network cohort, and 166 after 3 (±1) years were scored for RA (erosions, joint space narrowing (JSN)) and OA (JSN, osteophytes (OST)) using validated atlases. DAS28-P was the proportion of DAS28 attributed to patient-reported factors. Adjusted odds ratios were calculated using logistic regression.

Results

OA was common at baseline in early RA (40% hand and 48% foot) and associated with RA radiographic score. Higher baseline RA scores were associated with increasing age and ESR, and lower DAS28-P. OST scores were associated with higher age.

DAS28 and patient reported outcomes improved, whereas RA and OA radiographic scores deteriorated by follow up. Erosive progression was predicted by higher baseline erosions, female gender, better mental health and lower DAS28-P. Hand OST progression was predicted by baseline OST scores. Inflammatory disease activity was associated with erosive, but not with OA progression. Baseline hand OA predicted worse physical function at follow up, but radiographic progression did not explain changes in patient reported outcomes.

Discussion

OA is a common comorbidity that might confound radiographic and clinical assessment but does not fully explain erosive progression or patient-reported outcomes in early RA. Early RA management should address psychosocial factors and comorbidities, as well as joint inflammation.

Significance and Innovation

1. Radiographic OA is common in the hands and feet of those with early RA, and hand OA might confound RA assessment and influence clinical outcome.
2. RA and OA structural damage each might progress during the first 3 years after presentation with RA, despite significant improvements in DAS28 and patient reported outcomes.
3. Measures of the proportion of DAS28 contributed by tender joint counts and VAS-GH (DAS28-P), or mental health scores, might help stratify those at risk of rapid erosive progression.

Introduction

Osteoarthritis (OA) is prevalent in the ageing population, including those in whom RA first becomes apparent (1). OA might confound RA assessment, being a comorbid source of joint pain, and either diagnosis might moderate pathogenesis of the other disease. Inflammatory RA might suppress osteophytosis (2), whereas suppression of RA inflammation with biologics reduced structural OA (3).

The 28 joint Disease Activity Score (DAS28) is commonly used to measure inflammatory disease activity, and inform treatment/response decisions (4, 5). Although interpreted as a measure of inflammation, DAS28 is increased also in people with RA who have concurrent fibromyalgia (6). We have recently derived the DAS28-P index, which is the proportion of DAS28 attributed to patient-reported factors (7). DAS28-P was associated with higher TJC, VAS-GH, sensitivity to pain and worse pain progression in RA, as well as poorer mental health and fatigue scores (8).

This study aimed to elucidate associations between joint damage, inflammation, pain and disability in people with early RA, and explore how comorbid OA might influence patient assessment and outcomes.

Methods

Patients and Recruitment

The ERAN inception cohort (9, 10) recruited from outpatient centres in the UK and Eire (10, 11) 2002-2014. Patients were recruited following their first diagnosis of RA by a rheumatologist, and were not required to satisfy 1987 ACR RA criteria (46% at baseline and 45% at follow up fulfilled the criteria). Participants were monitored, treated and underwent radiography according to clinical need guided by schedule agreed by consensus prior to cohort recruitment. At baseline 41% were treated with methotrexate monotherapy, 25% sulphasalazine monotherapy and 24% a combination of non-biologic DMARDs . Glucorticoid use was reported in 19% of participants at baseline. ERAN was approved by Trent Research Ethics Committee (ref 01/4/047) and all participants gave signed, informed consent in line with the Declaration of Helsinki.

Data collection

Standardised demographic and disease activity data were collected at baseline, 3-6 months, 1 year and yearly from baseline thereafter. Seropositive was defined as positive or strongly positivity for rheumatoid factor or antibodies to citrullinated proteins using local laboratory ranges. Participants also completed Short Form 36 (SF36)(12) and Health Assessment (HAQ; disability index) (13) questionnaires. DAS28-P index was calculated as the proportion of DAS28 attributed to patient-reported factors (TJC and VAS-GH) in people with active RA (DAS28 > 3.2) (7).

Radiography

Plain radiographs of hands (anterior posterior) and feet (dorsoplantar) were collected from 6 centres with high recruitment to ERAN (Wye Valley NHS Trust, Sherwood Forest Hospitals NHS Foundation Trust, West Hertfordshire Hospitals NHS Trust, University Hospitals of Morecambe Bay NHS Foundation Trust, Yeovil District Hospital NHS Foundation Trust and North Bristol NHS Trust).

Radiographic images were from electronic data stores, or radiographic films were scanned using an Epson Expression® 10000XL (Seiko Epson, Japan). Participants were representative of those recruited at the selected ERAN centres for whom baseline radiographs were not collected (data not shown); baseline radiographic scores did not differ significantly between the patients attending different study centres (data not shown). Compared with those who only provided baseline images, people providing follow up images were older at baseline (mean 60 y vs 55 y, $p < 0.001$); had higher DAS28 (mean 4.8 vs 4.4, $p<0.036$) and were less likely to be current smokers (29% vs 41%; $p=0.012$). Baseline radiographic scores did not differ significantly between those that provided follow up images, and those that provided baseline only images (data not shown).

RA radiographic scoring

Images of hands and feet were scored for erosions and JSN using the van der Heijde modification of Sharp's method (14, 15) for erosions and JSN (16). Hand proximal interphalangeal (PIP) joints, MCP joints, carpo-metacarpal joints (CMC) 3-5, thumb base, radiocarpal joint, capitate-navicular-lunate joints, multangular navicular, trapezium/trapezoid metatarsophalangeal (MTP) and the hallux IP joints were assessed. Erosions were defined as regions with breakage or severe disruption of the intra-capsular marginal cortical bone. Summated erosion and JSN scores give a total ranging from 0 to 448 with a maximum erosion score of 280 and JSN score of 168 (17). A 5 point progression in total score within 1 year is considered clinically important (18).

Scoring was performed by one scorer (DMcW) who prior to the study was compared with an experienced scorer (KJ) (19) using 25 sets of hand and foot radiographs from the Early Rheumatoid Arthritis Study (ERAS) cohort (20). Intra-class correlation coefficients (ICC) for inter-observer variation were 0.80 (0.60 - 0.90) for erosions and 0.75 (0.57 - 0.86) for total/summated score ($p < 0.001$ for all). Intra-observer ICCs were 0.92 (0.82 – 0.97) and 0.95 (0.87 – 0.98) respectively.

OA radiographic scoring

Validated radiographic scoring methods were used for hands (21, 22) and feet (23). At both sites, osteophytes (OST) and JSN were scored on a scale of 0-3 with reference to a photographic atlas. For hand OA, scoring was performed for DIP joints, proximal interphalangeal (PIP) joints and the 1st carpo-metacarpal joint. Foot OA scoring was performed on MTP1, cuneo-metatarsal (CMT) joints 1 and 2, cuneo-navicular joint and talonavicular joint (JSN only). Additionally, hand OA was classified when a joint from the hand OA atlas showed Kellgren and Lawrence grade ≥2 (24), and grades were also recorded for thumb (interphalangeal and metacarpal) and MCP joints (digits 2-5). Foot OA was classified when any joint from the foot OA atlas showed an OST score ≥2 (23).

The single observer (DMcW) was compared to an experienced scorer (SD) using 20 pairs of hands from the GOAL study (25). Summated joint scores for the whole hand, DIP and PIP joints had inter-observer ICCs (95% CI) of 0.78 (0.53–0.91); 0.89 (0.74–0.95) and 0.78 (0.52–0.91) respectively ($p<0.001$). Intra-observer ICCs (95% CI) were 0.94 (0.72 – 0.96), 0.98 (0.93 – 0.99); and 0.98 (0.96 – 0.99), respectively. Foot OA scoring by the single scorer (DMcW) was compared to an experienced scorer (MM) using 60 pairs of feet from the CAS-F study (26). For summated OST scores, inter-observer ICC (95% CI) was 0.81 (0.69 – 0.89), and intra-observer ICC (95% CI) was 0.84 (0.58 – 0.94)).

ERAN study participants were assessed in a blinded, random order, with images from different centres randomly mixed. However, radiographs were viewed chronologically within each person (14). Baseline radiographs were within one calendar year of the baseline visit. A total of 512 people had at least one baseline radiograph which yielded 459 pairs of fully scoreable hands and feet at baseline. Follow up radiographs were selected from 3 (±1) year follow up time point giving a final sample size of 166 people with hand and foot radiographs scored at baseline and follow up.

Statistical analysis

Radiographic scores, and their progression were primary outcome variables, and complete case analysis was performed. Each outcome variable was divided by the median for calculation of odds ratios (OR), adjusted OR (aOR), and 95% confidence intervals (CI). Spearman's rank correlation coefficients were calculated for analysis during follow up. Baseline DAS28 scores were classified into EULAR disease activity groups (Low: 0-3.19 (for whom DAS28-P is not calculated (7)), moderate: 3.20-5.19, and high: ≥ 5.20)(27); BMI was classified into WHO groups (<25; 25.0-29.9; ≥30)(28). Other continuous variables were divided into tertiles of increasing severity. Univariate analyses were not adjusted for multiple comparisons. Logistic regression models were all adjusted for age, gender and either DAS28 (or all 4 DAS28 components) and length of follow up (2–3 years, or 3–4 years). Additionally, they were adjusted for those variables with p values<0.10 in univariate analysis . For cross-sectional logistic regression analyses of baseline only data, adjusting variables were selected (RA radiographic scores - DAS28-P; or ESR, SJC, TJC and VAS-GH, plus symptom duration (erosions only) or mental health (JSN only). Hand OA - DAS28-P, serology and symptom duration (all), plus mental health (OST only) or physical function (JSN only). Foot OA - DAS28-P (all), plus HAQ (OST only), or serology, mental health, bodily pain, vitality and physical function (JSN only). Analysis of baseline hand OA and disability at 3 years were adjusted for baseline disability measure (HAQ or SF36-Physical Function), age, gender and DAS28. Statistical analysis was performed using SPSS version 21 (IBM Corp, USA). Statistical significance was taken when $p < 0.05$.

Results

Demographics and clinical characteristics

Baseline characteristics of the study group are shown in Table 1.

Cross sectional associations of baseline radiographic scores

Radiographic scores are shown in Table 2. The median (IQR) RA score was 6 (4-12); the hand OST score was 9 (0-5); and the foot OST score was 2 (1-4). Patients with erosive changes on hand or foot radiographs displayed higher OA radiographic scores, both for OST and for JSN, both in hands and in feet (Table 2). Furthermore, OA was observed within DIP joints in 30% of cases, in PIP joints in 12% and in the thumb base in 13% of cases. In the foot, OA in MTP1 was observed in 44% of cases and CMT1 joint in 4% of cases. Evidence of OA was also observed in joints beyond the scope of the OA atlases, with OA in MCP joints in 19%; thumb IP joint in 15%; MTP2-5 in 6%; and hallux IP joints in 4% of cases. RA and OA radiographic changes were occasionally observed within the same joint (See Supplementary figure 1).

Univariate analyses were used to explore cross-sectional associations at baseline (Table 3). Age was consistently associated with higher radiographic scores and DAS28-P was associated with lower radiographic scores in most measures (Table 3). Symptom duration, serology, and ESR were also associated with some of the radiographic scores.

Further analysis at baseline was performed, using logistic regression to assess which factors were independently associated with baseline radiographic scores. Baseline erosions score was associated (aOR, (95% CI)) with age (2.57 (1.77 to 3.72)); longer duration (1.49 (1.06 to 2.29)); and lower DAS28-P (0.68 (0.48 to 0.97)). Analysis after the inclusion of ESR, SJC, TJC and VAS-GH, and removal of DAS28 and DAS28-P, showed that erosions were associated with higher ESR (1.77 (1.26 to 2.47), and lower TJC scores (0.63 (0.43 to 0.93). Similar analysis of OA at baseline showed that age was

independently associated with higher OST score (aOR 3.93 (95% CI 2.39 to 6.47), p<0.001). Higher OA JSN score in the hands was associated with greater age (aOR 3.37 (2.08 – 5.47), p<0.001) and female gender (aOR 2.36 (1.16 – 4.78), p=0.018). At baseline, age was associated with higher foot OST scores (aOR 3.02 (95% CI 2.11 to 4.34), p<0.001). Foot JSN scores were associated with age (aOR 1.93 (1.19 – 3.14), p=0.008) and female gender (aOR 2.16 (1.05 – 4.46), p=0.036).

Radiographic progression in early RA

At 3 (±1) year follow up there were n=166 cases that provided radiographic images with scores (median (IQR)) of total; 14 (7 – 23), erosions; 5 (2 – 10) and JSN; 7 (4 – 13). These represented increases of total; 6 (3 – 12), p<0.001; erosions; 3 (1 – 6) p<0.001, and JSN; 3 (1 – 7) p<0.001. 89% (148/166) of participants had one or more erosions in either hands (80%) or feet (65%), and people with erosions scored at follow up were significantly older than those without (mean age 57 vs 45 years, P<0.05). Radiographic OA scores (median (IQR)) at follow up were hand OST; 1 (0 - 7) and JSN; 1 (0 – 3), and foot OST; 2 (1 – 4) and JSN; 4 (3 – 5). Hand OST progressed by 0 (0 – 2), p<0.001 and foot OST by 0 (0 – 1), p<0.001. Hand OA JSN progressed 0 (0 - 1), p=0.046 and foot JSN by 1 (-1 – 2), p<0.001 (Table 2). At follow up, 41% (68/166) of participants were classified as having hand OA, and 47% (78/166) had foot OA. Hand OA and foot OA were newly classified at follow up in respectively 15% (17/111) and 25% (24/96) of participants who were not classified as having OA at baseline. Further examination of OA progression showed that those people without OST's at baseline in scored hand or foot joints progressed to KL score classification as hand OA or foot OA in 4% (4/92) and 3% (3/33) of cases respectively. Radiographs that were scored JSN=0 and OST=0 at baseline, were rare in those with OA at follow up. 1.4% (1/74) of those with hand OA at follow up had no JSN and no OST at baseline.

Predictors of radiographic progression in early RA

Table 4 presents the univariate analyses of baseline characteristics associated with greater changes in radiographic scores. Age and radiographic scores were the only baseline variables significantly associated with changes in total or JSN RA radiographic scores. Increases in erosion scores were associated with higher age, higher baseline erosion score, more hand OA, lower DAS28-P and better vitality and mental health (table 4). Changes in hand OST scores were predicted at the univariate level by higher age, higher baseline TJC, hand OST score and foot OST score (Table 4). Greater changes in foot OST scores were associated with baseline hand OST scores (table 4). Univariate analysis of OA JSN scores are shown in supplementary Table 1.

Multivariable logistic regression was used to examine the data for independent predictors of higher than median radiographic change. Above median increases in erosion scores were predicted by higher baseline erosions score, female gender, better mental health and lower DAS28-P (table 5). Greater than median OST score progression for the hands was predicted by baseline hand OST score only (Table 5).

Clinical associations of radiographic change in early RA

To investigate the contribution of inflammatory disease activity to radiographic progression, cumulative values for DAS28 or its components were calculated from baseline to year 2. Higher cumulative ESR was associated with greater RA radiographic progression, but not with OA progression (supplementary Table 2). Higher cumulative DAS28 or VAS-GH was each associated with increased JSN change for both RA hand and OA foot scores (supplementary Table 2). Progression of OST radiographic scores was not significantly associated with cumulative DAS28 or any of its components (supplementary Table 2).

At 3 year follow up, we investigated whether the presence of OA at baseline was associated with worse clinical outcome. Hand OA at baseline was associated with worse SF36-physical function at follow up (hand OA: 30(14) vs no hand OA 37 (15), p=0.001), and worse HAQ disability scores at

follow up (hand OA:1.1 (0.8) vs no hand OA 0.8 (0.7), p=0.015). Adjustments for confounders removed the significance of these associations (Physical Function β=-3.0 (95% CI -9.2 to 3.2, p=0.336 and HAQ β=0.2 (95% CI -0.1 to 0.4, p = 0.197)). Corresponding univariate or multivariable associations were not significant between baseline hand OA and bodily pain or DAS28, neither between foot OA classification and any clinical outcome. Furthermore, we investigated whether changes in radiographic scores may mediate clinical outcome in early RA. Progression of RA and OA radiographic scores were not significantly associated with worsening in SF36 Physical Function score, HAQ disability, or SF36 Bodily Pain score, even after adjusting for change in DAS28 (all standardised beta values <0.23, $p \geq 0.091$).

Discussion

We found that radiographic OA was common in early RA, and RA and OA structural progression both occured during the first 3 years after diagnosis. Associations between RA and OA structural changes indicate that comorbid OA might confound disease assessment in people with early RA. Inflammation might mediate erosive progression, but non-inflammatory factors measured using mental health scores and DAS28-P moderate the ability of DAS28 to predict erosive progression in early RA. Factors such as DAS28-P or mental health deserve investigation as novel stratification tools for treatments targeting radiographic progression in early RA.

Sustained inflammatory disease activity causes erosive progression in RA (29, 30). A majority (61%) of participants with follow-up radiographs displayed RA radiographic progression of a magnitude considered “clinically important” (18). This might reflect inadequate disease suppression by monotherapies commonly used at the time of patient recruitment (31), and selection bias for those with more active inflammatory disease. Previous attempts to predict erosive progression in RA have focussed on those factors anticipated to augment RA pathogenesis (38). Baseline radiographic scores predicted radiographic progression, supporting the early classification of patient subgroups as either

erosive/non-erosive (32), or either osteoarthritic/non-osteoarthritic. Inflammation, seropositive status and erosions have been associated early RA (33). However, high baseline inflammatory disease activity might be associated with a greater potential to respond to treatment (34) or a greater likelihood of allocation to more intensive treatment in routine clinical practice (31). Seropositivity and DAS28 were not independent predictors of subsequent radiographic progression in our study, and the relationship between damage and serology might be stronger in uncontrolled disease (35).

Higher DAS28-P and worse mental health might identify a group of patients with augmented central pain processing, such as those with RA and concurrent fibromyalgia (6, 7, 36) who display less structural damage than those with RA alone (37). Our findings highlight the importance of non-inflammatory mechanisms as moderators of disease assessment, and prediction of erosive progression might be improved by inclusion of DAS28-P and measures of mental health.

Our study confirms relationships between RA and OA radiographic features at baseline and their progression (1, 39). RA or OA radiographic scoring achieves specificity by inclusion of disease-characteristic joint groups (e.g. metacarpophalangeal (MCP) joints for RA and distal interphalangeal (DIP) joints for OA). Comparable with non-RA populations, the predominant joints affected by OA in our study were DIP (40) and 1st MTP joints (26)). However, either disease might affect joints that are scored for the other disease. Associations between RA and OA might reflect the propensity of both diseases to cause cartilage damage and JSN (14), or effects of age and other confounding factors. Prolonged synovitis and erosive damage might eventually lead to co-occurring OA (22), although this association was not apparent in this early RA cohort. Similarly, OA at baseline did not significantly moderate the risk of erosive damage over the same period. In summary, OA can be considered a comorbid condition in early RA. We show that comorbid OA might influence inflammatory disease

assessment in RA, for example by contributing to swollen joint counts in the hands, or to disability (foot OA).

Consistent with previous studies, radiographic OA was associated with increasing age (41) and increasing age was also associated with worse baseline RA radiographic scores (42).. Older patients might present with more advanced disease, perhaps because they might accept joint symptoms as a sign of normal ageing. Peak RA incidence has shifted to older age groups in recent decades, and the burden of concurrent RA and OA is likely to further increase. Lack of association between OA and BMI or gender might reflect study power or moderating effects of RA.

Interpretation of our data is subject to several methodological limitations. Radiographic scoring by a single observer eliminated inter-observer variability, but similar results might not be obtained by other investigators. RA and OA features were scored separately, with more than several weeks between scoring of the same films for respective diseases. However, scorers cannot be blinded to concurrent radiographic features. All cortical disruptions were scored as erosions (43), and uneven cortical bone surfaces adjacent to osteophytes might have influenced RA radiographic scoring. Scoring images in chronological sequence permits back-checking of difficult images, but knowing that all participants had early RA might have led us to overestimate radiographic progression.

ERAN documents a `real life' inception cohort of people who present to secondary care services with early RA and the frequency of radiographic assessment varied, although inclusion of follow up period as a covariate did not affect our conclusions. Study centre inclusion was not random, and follow up radiographs were available for only a subgroup which differed from the total ERAN population in baseline disease activity and smoking, both of which are risk factors for poor outcomes. Reported RA radiographic scores in the current study are comparable to previous reports (44), but higher than others (45, 46). Our included participants might have had worse clinical features and undergone more frequent radiographic follow up, and our findings may be representative of those with more

active RA. OA pathology might precede radiographic change (47), and few people progressed to newly classified OA. Our findings apply mainly to the progression of OA that was present at first presentation with RA, and further research should investigate whether the presence of early RA affects OA incidence.

In conclusion, OA is a common comorbidity in early RA, and both RA and OA structural progression occur during the first 3 years after diagnosis. Associations between RA and OA structural changes indicate the potential for comorbid OA to confound early RA disease assessment. Inflammation mediates erosive progression, but non-inflammatory factors moderate the ability of DAS28 to predict erosive progression in early RA. Holistic approaches to RA management are indicated, that address psychosocial factors and comorbidities, as well as joint inflammation.

Contributions: Study design and conception: DAW, AY, PDK, MD, WZ, DFM.

Data collection: DFM, MM, SD, KJ, AY

Data analysis: DFM, DAW

Writing, editing and critical appraisal of manuscript: All authors

Approval of final manuscript: All co-authors

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Table 1: Baseline demographic and clinical characteristics of study population

	All cases with baseline radiographs
Demographics	
n=	512
Female	65%
Age (years)	58 (48 - 69)
BMI ($kg.m^{-2}$)	26.8 (24.1 - 30.5)
Smoking history	62%
RA disease characteristics	
Duration (months)	6 (3 - 12)
Seropositive	62%
DAS28	4.6 (3.4 - 5.7)
VAS-GH (0-100mm)	40 (20 - 62)
TJC (0-28)	5 (1 - 11)
SJC (0-28)	4 (1 - 8)
ESR (mm/hr)	20 (11 -37)
CRP (ng/dL)	7 (3 - 20)
DAS28-P	0.45 (0.38 - 0.50)
Patient reported outcome measures	
HAQ (0-3)	1.0 (0.4 - 1.5)
SF36-Bodily pain	35 (11)
SF36-Physical Function	31 (15)
SF36-Vitality	43 (11)
SF36-Mental Health	47 (11)

Median (IQR) or percentage prevalence, with SF36 data presented as mean (sd). SF36 scores represent normed values, where normal UK population values are mean 50 (SD 10). Seropositive was defined as positive for rheumatoid factor and/or citrullinated proteins. Groups compared using Mann-Whitney U-tests and χ^2 tests. Significance denoted as * $p < 0.05$, ** $p<0.01$. BMI- body mass index, HAQ-health assessment questionnaire, DAS28-P – proportion of patient-reported components in the DAS28 index.

Table 2: Baseline radiographic scores in early RA (univariate comparisons)

	Study group	Erosions in hand or foot ≥1		Hand K≥L2 OA		Foot osteophyte scored >=2	
	Total	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**
Radiographic Scores							
Erosions	72%	0%	100%	65%	83% **	64%	81% **
RA score	6 (4 - 12)	2 (1 – 4)	8 (5 - 15)	4 (2 - 8)	11 (6 - 21) **	5 (2 - 8)	8 (4 - 16) **
Erosion score	2 (0 - 5)	0 (0 – 0)	3 (2 - 6)	1 (0 - 3)	3 (1 - 8) **	1 (0 - 3)	3 (1 - 6) **
JSN score (RA)	4 (2 - 8)	2 (1- 4)	5 (2 - 10) **	3 (1 - 5)	6 (4 - 12) **	3 (1 - 6)	5 (3 - 11) **
Hand OA	40%	24%	46% **	0%	100%	30%	52% **
Hand OST score	1 (0 - 5)	0 (0 - 2)	2 (0 - 6) **	0 (0 - 1)	6 (3 - 10) **	0 (0 - 3)	2 (0 - 6) **
Hand JSN score	1 (0 - 3)	0 (0 - 1)	1 (0 - 3) **	0 (0 - 1)	3 (1 - 6) **	0 (0 - 2)	1 (0 - 3) **
Foot OA	48%	33%	54% **	39%	61% **	0%	100%
Foot OST score	2 (1 - 4)	2 (0 - 3)	2 (1 - 4) **	2 (0 - 3)	3 (2 - 5) **	1 (0 - 2)	4 (3 - 5) **
Foot JSN score	4 (2 - 5)	3 (2 - 4)	5 (2 - 10) **	3 (2 - 5)	4 (3 - 6) **	3 (2 - 5)	4 (3 - 6) **

Baseline radiographic scores and radiographic classifications (median (IQR)) or percentage. ** p<0.01; * p<0.05 in Yes vs No comparisons (univariate, unadjusted analyses).

Table 3: Univariate associations between baseline radiographic scores and baseline patient and disease characteristics

		Rheumatoid arthritis scoring				Osteoarthritis scoring		
		Above median radiographic score	Above median erosions score	Above median JSN score	Above median hand OST score	Above median hand JSN score	Above median foot OST score	Above median foot JSN score
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographics								
Gender	Female	1.01 (0.69 - 1.49)	1.13 (0.77 - 1.66)	0.89 (0.61 - 1.32)	1.20 (0.83 - 1.75)	1.02 (0.70 - 1.48)	0.69 (0.47 - 1.01)	1.07 (0.73 - 1.58)
Age (years)	Low tertile	1	1	1	1	1	1	1
	Middle tertile	**2.40 (1.51 - 3.85)****	**2.63 (1.65 - 4.21)****	**2.41 (1.51 - 3.85)****	**5.16 (3.03 - 8.79)**	**2.83 (1.77 - 4.54)**	**5.10 (3.02 - 8.64)****	**1.91 (1.22 - 3.01)****
	High tertile	**9.13 (5.37 - 15.51)****	**6.61 (3.92 - 11.18)****	**9.85 (5.70 - 17.03)****	**18.06 (10.25 - 31.83)**	**15.33 (8.83 - 26.63)**	**6.78 (3.97 - 11.59)****	**3.80 (2.33 - 6.18)****
BMI ($kg.m^{-2}$)	<25	1	1	1	1	1	1	1
	25-29.99	0.96 (0.60 - 1.55)	1.12 (0.70 - 1.81)	1.26 (0.78 - 2.04)	1.02 (0.64 - 1.61)	0.83 (0.53 - 1.32)	1.23 (0.76 - 1.99)	**0.69 (0.43 - 1.11)**
	30+	0.93 (0.55 - 1.57)	1.07 (0.64 - 1.82)	1.05 (0.62 - 1.78)	0.98 (0.59 - 1.62)	1.11 (0.67 - 1.84)	1.21 (0.72 - 2.06)	**0.53 (0.31 - 0.89)***
Smoking history	Yes	0.99 (0.68 - 1.46)	1.19 (0.81 - 1.75)	0.97 (0.66 - 1.42)	0.93 (0.64 - 1.35)	0.79 (0.54 - 1.14)	1.30 (0.88 - 1.91)	0.87 (0.60 - 1.28)
Disease characteristics and RA measures								
Symptom duration (months)	Low tertile	1	1	1	1	1	1	1
	Middle tertile	0.76 (0.48 - 1.21)	0.70 (0.44 - 1.11)	0.77 (0.49 - 1.23)	0.64 (0.41 - 1.01)	0.57 (0.36 - 0.89)*	0.84 (0.53 - 1.33)	0.94 (0.60 - 1.50)
	High tertile	1.39 (0.88 - 2.18)	1.53 (0.96 - 2.43)	0.96 (0.61 - 1.52)	**0.56 (0.36 - 0.87)***	0.64 (0.41 - 1.00)	1.06 (0.68 - 1.67)	1.05 (0.67 - 1.65)
Serology	Positive	0.96 (0.63 - 1.47)	0.88 (0.57 - 1.35)	0.70 (0.45 - 1.07)	**0.58 (0.39 - 0.88)***	**0.62 (0.41 - 0.94)***	0.77 (0.51 - 1.18)	0.64 (0.42 - 0.99)
DAS28-ESR	<3.2	1	1	1	1	1	1	1
	3.2 - 5.19	0.76 (0.43 - 1.34)	0.86 (0.49 - 1.52)	0.77 (0.44 - 1.37)	0.91 (0.53 - 1.56)	0.99 (0.58 - 1.69)	0.93 (0.53 - 1.64)	0.81 (0.46 - 1.42)
	5.2+	0.93 (0.52 - 1.65)	1.18 (0.67 - 2.10)	0.80 (0.45 - 1.42)	1.20 (0.70 - 2.07)	1.52 (0.88 - 2.61)	1.28 (0.73 - 2.24)	0.68 (0.39 - 1.21)
VAS-GH (0-100mm)	Low tertile	1	1	1	1	1	1	1
	Middle tertile	0.82 (0.52 - 1.29)	0.69 (0.43 1.10)	**0.70 (0.44 - 1.11)**	0.79 (0.51 - 123)	0.69 (0.44 - 1.07)	0.85 (0.54 - 1.35)	0.78 (0.49 - 1.24)
	High tertile	0.81 (0.51 - 1.29)	0.84 (0.53 - 1.34)	**0.58 (0.36 - 0.93)***	0.76 (0.48 - 1.18)	0.74 (0.47 - 1.16)	0.89 (0.56 - 1.40)	**0.44 (0.28 - 0.71)****

TJC (0-28)	Low tertile	1	1	1	1	1	1	1
	Middle tertile	0.69 (0.44 - 1.08)	0.63 (0.40 - 1.00)	0.62 (0.39 0.98)	0.90 (0.58 - 1.40)	1.11 (0.72 - 1.72)	0.77 (0.49 - 1.21)	0.81 (0.51 - 1.27)
	High tertile	0.69 (0.43 - 1.09)	0.72 (0.45 - 1.14)	0.79 (0.50 - 1.24)	1.04 (0.68 - 1.61)	1.17 (0.76 - 1.80)	1.11 (0.71 - 1.75)	0.63 (0.40 - 1.00)
SJC (0-28)	Low tertile	1	1	1	1	1	1	1
	Middle tertile	1.13 (0.71 - 1.78)	1.20 (0.76 - 1.89)	1.01 (0.64 - 1.59)	1.41 (0.91 - 2.19)	1.31 (0.85 - 2.03)	0.90 (0.57 - 1.42)	0.85 (0.53 - 1.34)
	High tertile	1.41 (0.87 - 2.26)	1.53 (0.95 - 2.47)	1.09 (0.68 - 1.76)	**1.77 (1.11 - 2.81)***	1.58 (1.00 - 2.50)	1.41 (0.87 - 2.27)	0.73 (0.45 - 1.17)
ESR (mm/hr)	Low tertile	1	1	1	1	1	1	1
	Middle tertile	**1.91 (1.13 - 3.24)***	**2.87 (1.69 - 4.89)****	1.67 (1.00 2.81)	1.49 (0.90 - 2.46)	1.51 (0.92 - 2.48)	1.19 (0.70 - 2.00)	1.17 (0.69 - 1.96)
	High tertile	**2.44 (1.42 - 4.19)***	**3.37 (1.95 - 5.83)****	**1.82 (1.07 - 3.10)***	**2.05 (1.23 - 3.44)****	**2.64 (1.57 - 4.45)****	1.51 (0.89 - 2.54)	1.02 (0.61 - 1.70)
DAS28-P	Low tertile	1	1	1	1	1	1	1
	Middle tertile	**0.45 (0.25 - 0.82)***	**0.46 (0.25 - 0.85)***	**0.49 (0.27 - 0.89)***	0.62 (0.35 - 1.10)	0.57 (0.32 - 1.03)	1.00 (0.56 - 1.79)	0.84 (0.47 - 1.52)
	High tertile	**0.44 (0.24 - 0.80)***	**0.38 (0.21 - 0.69)****	**0.38 (0.21 - 0.70)****	**0.29 (0.16 - 0.52)****	**0.35 (0.19 - 0.63)****	0.61 (0.33 - 1.10)	**0.48 (0.26 - 0.86)***
Patient reported outcome measures								
HAQ (0-3)	Low tertile	1	1	1	1	1	1	1
	Middle tertile	0.78 (0.49 - 1.24)	0.93 (0.59 - 1.48)	0.74 (0.46 - 1.19)	0.79 (0.50 - 1.23)	0.85 (0.54 - 1.32)	1.31 (0.82 - 2.10)	0.69 (0.43 - 1.10)
	High tertile	0.94 (0.59 - 1.50)	0.94 (0.59 - 1.49)	0.93 (0.58 - 1.49)	1.08 (0.69 - 1.70)	1.29 (0.82 - 2.03)	**1.72 (1.07 - 2.76)***	0.67 (0.42 - 1.08)
SF36-Bodily Pain	Good tertile	1	1	1	1	1	1	1
	Middle tertile	1.09 (0.65 - 1.83)	0.74 (0.44 - 1.25)	1.12 (0.66 - 1.90)	0.78 (0.48 - 1.29)	0.92 (0.56 - 1.51)	0.81 (0.48 - 1.37)	0.65 (0.38 - 1.11)
	Poor tertile	1.00 (0.60 - 1.66)	0.78 (0.47 - 1.30)	0.67 (0.40 - 1.12)	0.92 (0.56 - 1.52)	0.77 (0.47 - 1.27)	1.09 (0.65 - 1.83)	**0.43 (0.25 - 0.73)****
SF36-Physical function	Good tertile	1	1	1	1	1	1	1
	Middle tertile	1.18 (0.70 - 1.97)	1.05 (0.63 - 1.75)	1.43 (0.85 - 2.38)	1.29 (0.79 - 2.10)	1.59 (0.97 - 2.59)	1.03 (0.62 - 1.71)	0.62 (0.37 - 1.05)
	Poor tertile	1.53 (0.92 - 2.56)	1.23 (0.74 - 2.06)	1.52 (0.91 - 2.54)	1.45 (0.89 - 2.37)	1.52 (0.93 - 2.48)	1.18 (0.71 - 1.96)	0.69 (0.41 - 1.15)
SF36-Vitality	Good tertile	1	1	1	1	1	1	1
	Middle tertile	1.02 (0.62 - 1.70)	1.08 (0.64 - 1.80)	0.87(0.52 - 1.46)	0.87 (0.53 - 1.41)	1.08 (0.66 - 1.75)	1.42 (0.86 - 2.37)	0.65 (0.39 - 1.08)
	Poor tertile	1.17 (0.70 - 1.95)	0.98 (0.58 - 1.63)	0.76 (0.46 - 1.28)	1.05 (0.64 - 1.72)	1.19 (0.73 - 1.94)	1.10 (0.66 - 1.85)	**0.54 (0.32 - 0.91)***

SF36-Mental health	Good tertile	1	1	1	1	1	1	1
	Middle tertile	0.87 (0.52 - 1.43)	0.83 (0.50 - 1.38)	0.66 (0.40 - 1.10)	0.63 (0.39 - 1.02)	0.67 (0.41 - 1.09)	0.72 (0.44 - 1.19)	0.62 (0.38 - 1.04)
	Poor tertile	0.95 (0.57 - 1.57)	0.74 (0.44 - 1.22)	0.61 (0.36 - 1.01)	0.79 (0.49 - 1.28)	0.66 (0.41 - 1.07)	0.86 (0.52 - 1.43)	**0.46 (0.28 - 0.77)****

Baseline radiographic variables and their univariate, unadjusted associations with demographic and clinical measures. Baseline radiographic scores were dichotomised into above and below median for generation of odds ratios (OR) and 95% confidence intervals (CI). The risks for above median scores are shown. Variables with a statistically significant result are highlighted in bold. ** $p<0.01$, * $p<0.05$.

Table 4: Radiographic progression in early RA (univariate analyses)

Erosions and osteophytes		Above/below median change in erosion score (2-4yr)	Above/below median change in hand OST score	Above/below median change in Foot OST
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographics				
Gender	Female	1.10 (0.58 – 2.08)	0.99 (0.52 - 1.87)	1.39 (0.73 - 2.67)
Age (years)	Low tertile	1	1	1
	Middle tertile	**2.55 (1.18 – 5.51)** *	1.85 (0.84 - 4.09)	0.79 (0.37 - 1.70)
	High tertile	**3.68 (1.66 – 8.15)** **	**3.72 (1.70 - 8.15)****	1.57 (0.73 - 3.35)
BMI ($kg.m^{-2}$)	<25	1	1	1
	25-29.99	1.19 (0.55 - 2.57)	1.05 (0.49 - 2.24)	1.24 (0.57 - 2.70)
	30+	1.05 (0.45 - 2.45)	1.35 (0.59 - 3.10)	1.20 (0.51 - 2.86)
Smoking history	Yes	0.89 (0.47 - 1.68)	0.72 (0.38 - 1.34)	0.57 (0.30 - 1.07)
Disease Characteristics and RA measures				
Symptom duration (months)	Low tertile	1	1	1
	Middle tertile	1.05 (0.47 - 2.34)	1.29 (0.60 - 2.77)	0.95 (0.44 - 2.04)
	High tertile	1.88 (0.88 - 4.01)	1.34 (0.62 - 2.87)	0.85 (0.39 - 1.88)
Serology	Seropositive	1.85 (0.87 - 3.92)	0.74 (0.35 - 1.55)	1.11 (0.52 - 2.38)
DAS28-ESR	<3.2	1	1	1
	3.2 - 5.19	2.13 (0.79 - 5.69)	1.00 (0.38 - 2.64)	1.22 (0.46 - 3.22)
	5.2+	2.57 (0.95 - 6.98)	1.84 (0.70 - 4.82)	1.59 (0.61 - 4.15)
VAS-GH (0-100mm)	Low tertile	1	1	1
	Middle tertile	0.66 (0.30 - 1.42)	0.48 (0.22 - 1.03)	0.69 (0.32 - 1.48)
	High tertile	0.83 (0.39 - 1.75)	0.64 (0.31 - 1.33)	0.63 (0.29 - 1.35)
TJC (0-28)	Low tertile	1	1	1
	Middle tertile	1.75 (0.83 - 3.71)	1.94 (0.88 - 4.25)	1.21 (0.56 - 2.61)
	High tertile	0.96 (0.44 - 2.08)	**2.91 (1.32 - 6.41)***	1.16 (0.54 - 2.52)
SJC (0-28)	Low tertile	1	1	1
	Middle tertile	1.65 (0.77 - 3.50)	1.24 (0.58 - 2.66)	0.96 (0.45 - 2.09)
	High tertile	1.56 (0.74 - 3.26)	1.36 (0.66 - 2.77)	1.34 (0.64 - 2.79)
ESR (mm/hr)	Low tertile	1	1	1
	Middle tertile	1.50 (0.65 - 3.48)	0.85 (0.37 - 1.94)	1.43 (0.62 - 3.26)
	High tertile	2.13 (0.94 - 4.82)	1.29 (0.58 - 2.85)	1.26 (0.55 - 2.88)
CRP (ng/dL)	Low tertile	1	1	1
	Middle tertile	0.81 (0.31 - 2.17)	1.42 (0.50 - 4.08)	0.72 (0.27 - 1.97)
	High tertile	1.00 (0.39 - 2.59)	1.25 (0.48 - 3.25)	1.77 (0.67 - 4.67)
DAS28-P	Low tertile	1	1	1
	Middle tertile	0.46 (0.18 – 1.17)	0.41 (0.17 - 1.00)	1.00 (0.41 - 2.47)
	High tertile	**0.33 (0.13 – 0.85)** *	0.81 (0.34 - 1.98)	0.77 (031 - 1.92)
Outcome Measures				

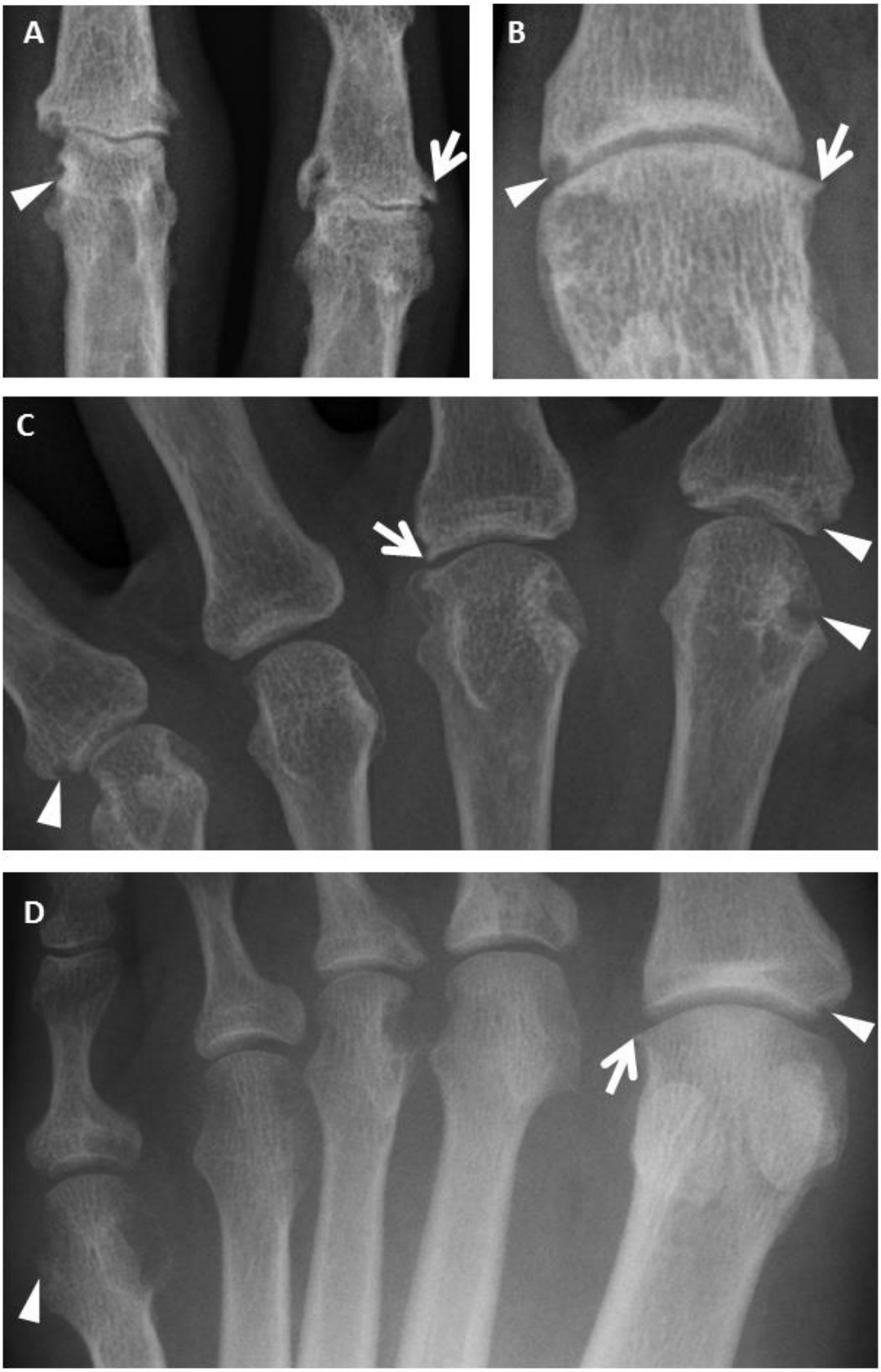
HAQ (0-3)	Low tertile	1	1	1
	Middle tertile	1.17 (0.53 - 5.59)	1.41 (0.65 - 3.06)	0.99 (0.46 - 2.14)
	High tertile	0.93 (0.44 - 1.96)	1.06 (0.48 - 2.36)	0.59 (0.26 - 1.33)
SF36-Bodily Pain	Good tertile	1	1	1
	Middle tertile	1.06 (0.44 - 2.58)	0.81 (0.37 - 1.77)	0.54 (0.24 - 1.22)
	Poor tertile	0.47 (0.20 - 1.07)	1.03 (0.42 - 2.50)	0.68 (0.27 - 1.69)
SF36-Physical function	Good tertile	1	1	1
	Middle tertile	1.23 (0.52 - 2.91)	1.30 (0.58 - 2.90)	1.41 (0.61 - 3.24)
	Poor tertile	0.66 (0.29 - 1.49)	1.00 (0.44 - 2.27)	1.06 (0.45 - 2.50)
SF36-Vitality	Good tertile	1	1	1
	Middle tertile	0.50 (0.21 - 1.16)	1.28 (0.57 - 2.89)	0.51 (0.22 - 1.19)
	Poor tertile	**0.39 (0.16 - 0.94)** *	0.84 (0.36 - 1.95)	1.05 (0.44 - 2.48)
SF36-Mental health	Good tertile	1	1	1
	Middle tertile	0.68 (0.29 - 1.55)	0.64 (0.29 - 1.43)	0.46 (0.20 - 1.05)
	Poor tertile	**0.28 (0.12 - 0.68)** **	0.65 (0.28 - 1.47)	0.95 (0.41 - 2.21)
Radiographic scores				
RA total score	Low tertile	1	1	1
	Middle tertile	**2.42 (1.12 - 5.20)***	1.31 (0.61 - 2.81)	1.19 (0.55 - 2.57)
	High tertile	**5.47 (2.44 - 12.27)****	2.22 (1.03 - 4.78)	1.57 (0.73 - 3.40)
Erosion score	Low tertile	1	1	1
	Middle tertile	1.65 (0.77 - 3.58)	1.31 (0.60 - 2.85)	0.70 (0.32 - 1.52)
	High tertile	**4.59 (2.01 - 10.50)****	1.95 (0.89 - 4.31)	1.18 (0.54 - 2.59)
Hand OST	Low tertile	1	1	1
	Middle tertile	2.72 (1.17 - 6.32)	2.15 (0.93 - 4.96)	**0.31 (0.12 - 0.83)***
	High tertile	1.75 (0.86 - 3.58)	**7.19 (3.35 - 15.43)****	**2.16 (1.04 - 4.50)***
Foot OST	Low tertile	1	1	1
	Middle tertile	0.94 (0.46 - 1.91)	2.15 (0.93 - 4.96)	0.65 (0.32 - 1.32)
	High tertile	1.46 (0.64 - 3.33)	**7.19 (3.35 - 15.43)****	0.62 (0.28 - 1.37)

Baseline variables and their univariate, unadjusted associations with progression of erosions and osteophyte scores in those that provided follow up images. Follow up radiographic change scores were dichotomised into above and below median for generation of odds ratios (OR) and 95% confidence intervals (CI). The risks for above median changes are shown. Structural change divided into above/below median and OR (95% CI) calculated. Variables with significant results highlighted in **bold**. ** $p<0.01$, * $p<0.05$.

Table 5: Logistic regression for structural change in early RA

	Erosive progression (hands and feet)		Hand osteophyte progression		Foot osteophyte progression	
	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p
Age (years)	1.76 (0.64 - 4.80)	0.271	0.78 (0.35 - 1.72)	0.532	1.31 (0.53 - 3.22)	0.555
Female	**4.54 (1.28 - 16.08)**	**0.019**	0.77 (0.29 - 2.03)	0.599	2.14 (0.75 - 6.09)	0.158
DAS28	1.19 (0.34 - 4.19)	0.789	1.78 (0.68 - 4.68)	0.241	1.17 (0.40 - 3.43)	0.782
SF36-Bodily Pain	0.86 (0.39 - 1.89)	0.713	Not used		Not used	
SF36-Mental health	**0.45 (0.20 - 1.00)**	**0.049**	Not used		Not used	
SF36-Vitality	1.25 (0.51 - 3.01)	0.629	Not used		Not used	
DAS28-P	**0.45 (0.22 - 0.90)**	**0.025**	0.77 (0.42 - 1.41)	0.396	1.36 (0.71 - 2.59)	0.350
RA radiographic score	Not used		0.85 (0.47 - 1.54)	0.598	1.38 (0.71 - 2.67)	0.343
Erosions	**2.14 (1.02 - 4.50)**	**0.044**	Not used		Not used	
Hand OST	0.68 (0.30 - 1.55)	0.354	**2.46 (1.26 - 4.80)**	**0.008**	1.16 (0.59 - 2.31)	0.670
Foot OST	0.89 (0.44 - 1.83)	0.757	1.15 (0.62 - 2.14)	0.652	0.64 (0.32 - 1.26)	0.197
Duration of follow up (years)	1.15 (0.39 - 3.35)	0.802	1.09 (0.41 - 2.93)	0.865	1.83 (0.64 - 5.17)	0.257

Logistic regression models, adjusted for baseline factors and the risk of higher than median progression of erosions and osteophytes (n=166). Significant results highlighted in **bold**.


A
B
C
D

Supplementary figure 1: Selected radiographic images from different people showing coexistence of erosions and osteophytes. A. Proximal interphalangeal joints with erosions and osteophytes. B. 1st metatarso-phalangeal joint with evidence of osteophytosis and erosion formation. C. Metacarpo-phalangeal joints showing erosions and visible osteophytes (OA was not scored for this joint group). D. Metatarso-phalangeal joints with erosions visible and osteophyte in the first joint. Arrows denote osteophytes. Arrow heads denote erosions.

Supplementary table1: Clinical and demographic associations of joint space narrowing progression in early RA

Joint space narrowing		Above/below median change in Sharp/van der Heijde JSN score for hands and feet (2-4yr)		Above/below median change in Altman OA Hand JSN score		Above/below median change in Menz OA Foot JSN score	
		OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Demographics							
Gender	Female	0.82 (0.43 - 1.55)	0.623	1.48 (0.71 - 3.09)	0.367	1.12 (0.59 - 2.13)	0.747
Age	Low tertile	**1**		**1**		1	
	Middle tertile	**1.64 (0.76 - 3.52)**	**0.247**	**1.46 (0.60 - 3.54)**	**0.504**	0.89 (0.42 - 1.87)	0.849
	High tertile	**3.13 (1.43 – 6.86)**	**0.007**	**2.43 (1.05 - 5.66)**	**0.041**	0.64 (0.30 - 1.37)	0.336
BMI	<25	1		1		1	
	25-29.99	0.60 (0.28 - 1.31)	0.239	0.60 (0.26 - 1.38)	0.285	1.36 (0.64 - 2.92)	0.444
	30+	1.06 (0.45 - 2.48)	>0.999	0.75 (0.30 - 1.87)	0.647	1.41 (0.60 - 3.33)	0.515
Smoking history	Yes	1.53 (0.80 - 2.91)	0.256	1.24 (0.61 - 2.51)	0.599	1.28 (0.68 - 2.40)	0.519
Disease Characteristics and RA measures							
Symptom duration	Low tertile	1		1		1	
	Middle tertile	0.58 (0.26 - 1.31)	0.224	0.50 (0.22 - 1.17)	0.137	1.16 (0.54 - 2.49)	0.845
	High tertile	0.92 (0.44 - 1.95)	0.851	0.65 (0.29 - 1.46)	0.308	2.11 (0.95 - 4.67)	0.075
Serology	Seropositive	1.64 (0.77 - 3.50)	0.256	1.71 (0.70 - 4.17)	0.280	0.98 (0.46 - 2.08)	>0.99
DAS28-ESR	<3.2	1		1		1	
	3.2 - 5.19	0.90 (0.35 - 2.32)	>0.999	3.58 (0.96 - 13.83)	0.062	1.98 (0.77 - 5.13)	0.235
	5.2+	1.66 (0.64 - 4.33)	0.338	2.97 (0.78 - 11.24)	0.160	1.55 (0.60 - 3.96)	0.479
VAS-GH	Low tertile	1		1		1	
	Middle tertile	0.94 (0.43 - 2.05)	>0.99	1.03 (0.44 - 2.40)	>0.99	0.74 (034 - 1.58)	0.445
	High tertile	1.85 (0.87 - 3.94)	0.130	1.36 (0.61 - 3.04)	0.542	0.95 (0.44 - 2.01)	>0.99
TJC	Low tertile	1		1		1	

	Middle tertile	1.17 (0.55 - 2.46)	0.708	2.32 (0.97 - 5.52)	0.061	0.73 (0.34 - 1.57)	0.446
	High tertile	1.04 (0.48 - 2.25)	>0.99	1.64 (0.67 - 4.02)	0.370	0.82 (0.38 - 1.75)	0.698
SJC	Low tertile	1		**1**		1	
	Middle tertile	0.89 (0.42 - 1.90)	0.848	**0.86 (0.34 - 2.17)**	**0.818**	0.88 (0.41 - 1.87)	0.847
	High tertile	1.84 (0.87 - 3.87)	0.135	**2.39 (1.10 - 5.22)**	**0.033**	0.78 (0.38 - 1.61)	0.579
ESR (mm/hr)	Low tertile	**1**		**1**		1	
	Middle tertile	**1.49 (0.64 - 3.46)**	**0.395**	**2.02 (0.75 - 5.45)**	**0.217**	0.54 (0.24 - 1.24)	0.212
	High tertile	**2.54 (1.12 - 5.78)**	**0.040**	**3.04 (1.18 - 7.84)**	**0.024**	1.46 (0.65 - 3.30)	0.412
CRP (ng/dL)	Low tertile	1		1		1	
	Middle tertile	1.65 (0.61 - 4.47)	0.448	2.26 (0.73 - 6.94)	0.169	1.07 (0.41 - 2.82)	>0.99
	High tertile	1.77 (0.67 - 4.67)	0.327	1.00 (0.39 - 2.59)	>0.99	2.70 (1.00 - 7.26)	0.055
DAS28-P	Low tertile	1		1		1	
	Middle tertile	1.73 (0.69 – 4.38)	0.350	0.93 (0.37 - 2.31)	>0.99	0.73 (0.30 - 1.80)	0.647
	High tertile	0.57 (0.23 – 1.45)	0.346	0.58 (0.21 - 1.55)	0.326	1.29 (0.53 - 3.19)	0.649
Outcome Measures							
HAQ	Low tertile	1		1		1	
	Middle tertile	1.39 (0.62 - 3.11)	0.538	1.41 (0.57 - 3.49)	0.503	1.12 (0.52 - 2.41)	0.845
	High tertile	2.19 (1.03 - 4.68)	0.057	2.06 (0.85 - 5.04)	0.128	1.13 (0.51 - 2.51)	0.840
SF36-Bodily Pain	Good tertile	1		1		1	
	Middle tertile	1.57 (0.65 - 3.77)	0.377	0.83 (0.34 - 2.06)	0.816	1.23 (0.55 - 2.76)	0.682
	Poor tertile	0.89 (0.39 - 2.02)	0.836	1.64 (0.63 - 4.32)	0.336	0.85 (0.35 - 2.12)	0.819
SF36-Physical function	Good tertile	1		1		1	
	Middle tertile	0.90 (0.38 - 2.13)	0.830	1.27 (0.53 - 3.04)	0.660	1.13 (0.50 - 2.57)	0.835
	Poor tertile	1.29 (0.57 - 2.92)	0.679	0.71 (0.27 - 1.82)	0.632	1.15 (0.49 - 2.66)	0.831
SF36-Vitality	Good tertile	1		1		1	
	Middle tertile	1.32 (0.58 - 3.02)	0.535	2.23 (0.82 - 6.04)	0.153	2.26 (0.98 - 5.21)	0.063
	Poor tertile	1.06 (0.45 - 2.52)	>0.999	2.21 (0.80 - 6.10)	0.145	1.71 (0.72 - 4.08)	0.275
SF36-Mental health	Good tertile	1		1		1	
	Middle tertile	1.48 (0.65 - 3.35)	0.409	2.82 (1.09 - 7.30)	0.041	0.99 (0.44 - 2.24)	>0.99

	Poor tertile	0.77 (0.33 - 1.79)	0.669	1.68 (0.61 - 4.59)	0.449	0.88 (0.38 - 2.05)	0.831
Radiographic scores							
RA total score	Low tertile	**1**		1		1	
	Middle tertile	**2.42 (1.12 - 5.20)**	**0.035**	2.51 (1.07 - 5.93)	0.037	1.20 (0.56 - 2.58)	0.700
	High tertile	**3.56 (1.64 - 7.75)**	**0.001**	1.90 (0.77 - 4.59)	0.185	0.84 (0.39 - 1.79)	0.700
Erosion score	Low tertile	**1**		1		1	
	Middle tertile	**2.67 (1.20 - 5.91)**	**0.020**	1.76 (0.73 - 4.26)	0.277	0.95 (0.44 - 2.03)	>0.99
	High tertile	**4.05 (1.77 - 9.23)**	**0.001**	1.90 (0.78 - 4.64)	0.188	1.08 (0.49 - 2.37)	>0.99
JSN score	Low tertile	1		1		1	
	Middle tertile	1.58 (0.77 - 3.27)	0.270	1.25 (0.55 - 2.87)	0.674	1.24 (0.60 - 2.60)	0.578
	High tertile	2.25 (1.03 - 4.90)	0.052	1.93 (0.83 - 4.49)	0.138	0.98 (0.44 - 2.15)	>0.99
Hand OST	Low tertile	**1**		**1**		1	
	Middle tertile	**0.78 (0.34 - 1.78)**	**0.677**	**2.64 (1.08 - 6.45)**	**0.050**	0.61 (0.27 - 1.39)	0.298
	High tertile	**2.72 (1.30 - 5.70)**	**0.011**	**3.67 (1.70 - 7.92)**	**0.001**	0.97 (0.47 - 1.99)	>0.99
Hand JSN	Low tertile	**1**		**1**		1	
	Middle tertile	**1.06 (0.45 - 2.52)**	**>0.99**	**1.84 (0.71 - 4.75)**	**0.210**	0.97 (0.42 - 2.27)	>0.99
	High tertile	**2.39 (1.17 - 4.85)**	**0.022**	**2.35 (1.14 - 4.88)**	**0.026**	1.15 (0.57 - 2.34)	0.722
Foot OST	Low tertile	1		**1**		1	
	Middle tertile	2.04 (0.99 - 4.21)	0.068	**2.64 (1.08 - 6.45)**	**0.050**	1.12 (0.55 - 2.28)	0.857
	High tertile	2.10 (0.92 - 4.82)	0.095	**3.67 (1.70 - 7.92)**	**0.001**	0.60 (0.28 - 1.32)	0.237
Foot JSN	Low tertile	1		**1**		**1**	
	Middle tertile	1.49 (0.71 - 3.11)	0.351	**1.84 (0.71 - 4.75)**	**0.210**	**0.31 (0.14 - 0.69)**	**0.004**
	High tertile	1.68 (0.75 - 3.79)	0.225	**2.35 (1.14 - 4.88)**	**0.026**	**0.12 (0.05 - 0.28)**	**<0.001**

Univariate analysis of baseline variables associated with progression of joint space narrowing scores. Structural change divided into above/below median and OR (95% CI) calculated. Significant results highlighted in **bold**.

Supplementary Table 2: Univariate associations between cumulative DAS28 components (from 0 to 2 years) and radiographic progression

		Rheumatoid arthritis			Osteoarthritis			
		Total change	Erosions change	JSN change	Hand OST change	Hand JSN change	Foot OST change	Foot JSN change
	Tertile	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
DAS28	1	1	1	1	1	1	1	1
	2	2.92 (0.88 - 9.67)	**3.52 (1.05 - 11.83) ***	2.05 (0.63 - 6.69)	1.63 (0.49 - 5.34)	3.04 (0.78 - 11.81)	1.67 (0.48 - 5.74)	2.08 (0.59 - 7.38)
	3	2.19 (0.69 - 6.93)	2.19 (0.69 - 6.93)	**3.54 (1.09 - 11.51) ***	1.12 (0.35 - 3.59)	1.21 (0.29 - 5.01)	1.53 (0.48 - 4.88)	**5.83 (1.71 - 19.90) ****
ESR	1	1	1	1	1	1	1	1
	2	1.00 (0.31 - 3.22)	**4.20 (1.23 - 14.37) ***	0.49 (0.15 - 1.60)	1.60 (0.49 - 5.29)	0.94 (0.23 - 3.85)	1.30 (0.40 - 4.24)	1.56 (0.48 - 5.06)
	3	**5.00 (1.45 - 17.27) ***	**7.29 (2.03 - 26.10) ****	**4.49 (1.26 - 16.01) ***	1.60 (0.49 - 5.29)	2.62 (0.72 - 9.54)	0.58 (0.17 - 2.05)	1.56 (0.48 - 5.06)
SJC	1	1	1	1	1	1	1	1
	2	1.15 (0.54 - 3.93)	1.46 (0.54 - 3.90)	1.30 (0.48 - 3.52)	1.92 (0.68 - 5.46)	0.88 (0.26 - 2.91)	0.95 (0.33 - 2.72)	1.42 (0.51 - 3.96)
	3	1.85 (0.70 - 4.92)	1.13 (0.43 - 2.98)	2.69 (1.00 - 7.28)	1.50 (0.53 - 4.21)	1.71 (0.56 - 5.21)	1.86 (0.67 - 5.15)	2.71 (0.96 - 7.64)
TJC	1	1	1	1	1	1	1	1
	2	0.69 (0.26 - 1.82)	0.55 (0.21 - 1.46)	0.87 (0.33 - 2.30)	2.35 (0.84 - 6.60)	1.80 (0.62 - 5.25)	1.42 (0.51 - 3.97)	0.72 (0.26 - 1.98)
	3	0.89 (0.34 - 2.34)	0.48 (0.18 - 1.29)	1.85 (0.70 - 4.92)	1.57 (0.57 - 4.34)	0.49 (0.14 - 1.68)	1.51 (0.54 - 4.24)	2.00 (0.71 - 5.68)
VAS-GH	1	1	1	1	1	1	1	**1**
	2	1.75 (0.66 - 4.69)	1.06 (0.40 - 2.82)	**3.93 (1.39 - 11.12) ***	1.23 (0.45 - 3.37)	1.16 (0.40 - 3.40)	1.82 (0.66 - 5.04)	1.08 (0.39 - 2.96)
	3	1.55 (0.58 - 4.15)	0.51 (0.19 - 1.36)	**3.07 (1.09 - 8.60) ***	0.78 (0.28 - 2.17)	0.65 (0.21 - 2.05)	0.87 (0.31 - 2.46)	**3.60 (1.22 - 10.64) ***

Univariate analysis of cumulative DAS28, and its components, from people with baseline, 1 and 2 year data available. Cumulative DAS28, ESR, SJC, TJC and VAS-GH were compared to radiographic progression rates. ** $p<0.01$, * $p<0.05$.

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