EXTENDED REPORT

Lumbar disc degeneration: association between osteophytes, end-plate sclerosis and disc space narrowing

Stephen R Pye, David M Reid, Mark Lunt, Judith E Adams, Alan J Silman, Terence W O'Neill

Ann Rheum Dis 2007;**66**:330–333. doi: 10.1136/ard.2006.052522

See end of article for authors' affiliations

Correspondence to: Dr T W O'Neill, arc Epidemiology Unit, The University of Manchester, Oxford Road, Manchester M13 9PT, UK; terence.o'neill@manchester.ac.uk

Accepted 26 September 2006
Published Online First 6 October 2006

Background: Lumbar disc degeneration is characterised radiologically by the presence of osteophytes, end-plate sclerosis and disc space narrowing.
Aim: To determine the strength of the association between increasing severity of combinations of these features in a population sample of men and women.
Methods: Men and women aged ⩾50 years were recruited from a primary care-based community health index in Aberdeen, UK. Participants had lateral spinal radiographs performed according to a standard protocol. The intervertebral disc spaces (L1/2–L4/5) were evaluated for the presence of anterior osteophytes, end-plate sclerosis and disc space narrowing using a graded semiquantitative score (grade 0–3). Log linear modelling was used to determine the associations (pairwise) between increasing severity of these features, with the results expressed as β coefficients and 95% confidence intervals (CIs).
Results: There were 286 men (mean age 65.3 years) and 299 women (mean age 65.2 years) with spinal radiographs, yielding a total of 2340 assessable lumbar vertebral levels. In all, 73% of vertebral levels had evidence of osteophytes, 26% of sclerosis and 37% of disc space narrowing. Increasing severity of osteophyte grade was associated with an increasing severity both of sclerosis and of disc space narrowing, whereas the severity of sclerosis was associated with the severity of narrowing. This was true at all vertebral levels. The strongest association, however, was between osteophytes and sclerosis (β coefficient = 2.7, 95% CI 2.4 to 3.1). For sclerosis and narrowing the β coefficient was 1.9 (95% CI 1.7 to 2.1), whereas for osteophytes and narrowing the β coefficient was much weaker at 1.2 (95% CI 1.1 to 1.3). There was no important influence of vertebral level on any of these associations.
Conclusion: The association between increasing severity of osteophytes and end-plate sclerosis is stronger than for other combinations of radiographic features of lumbar disc degeneration.

Peripheral joint osteoarthritis is characterised radiologically by the presence of osteophytes, subchondral sclerosis and joint space narrowing. Joint space narrowing is due to cartilage loss, whereas both subchondral sclerosis and osteophytes are hypertrophic responses of bone, thought to arise directly either to cartilage loss or to biomechanical stress. The pathophysiology and hence the inter-relationship of these features are however not well understood. Recently, strong associations between the presence of enthesophytes, osteophytes and bone sclerosis at various joint sites have been shown.[1] Partly on the basis of these observations, it has been suggested that some individuals may be more likely to develop bone formation in response to disease occurrence.[2] We looked at a series of lumbar spine radiographs and characterised the severity of the component radiographic features. Although the pathology of disc degeneration differs from peripheral joint osteoarthritis, we hypothesised that if there was a predisposition to develop new bone formation in the form of osteophyte or sclerosis in response to mechanical stress, there would be a strong association between increasing severity of the features of new bone formation. The aim of this study was to determine the strength of the association between increasing severity of osteophytes and end-plate sclerosis, and the association between both these features and disc space narrowing in the lumbar spine.

METHODS

The subjects included in this analysis were recruited for participation in a screening survey of vertebral osteoporosis in Aberdeen, Scotland, UK.[3] The sampling frame was a community health index based on primary-care registrants.[4] Stratified random sampling was used with the aim of recruiting equal numbers of men and women in each of six 5-year age bands: 50–54, 55–59, 60–64, 65–69, 70–74 and ⩾75 years. Subjects were invited by letter to attend for lateral spinal radiographs, which were taken according to a standard protocol. For the lumbar spine, the film focus was centred on the second lumbar vertebra. All individuals gave written informed consent to taking part in the study, which also received the approval of the local ethics committee.

In all, 585 lumbar radiographs were available for review. Each vertebral level from L1/2 to L4/5 was assessed by a single observer for the presence and severity of osteophytes (anterior), end-plate sclerosis and vertebral narrowing, using a reference atlas and semiquantitative score (0 = none; 1 = mild; 2 = moderate; 3 = severe). In the atlas, images were chosen to illustrate the cut-points for changes in score. The intraobserver reproducibility had been assessed by the same observer who re-evaluated 60 films within 1 week of the first reading. The κ score, a measure of agreement, was 0.83 for osteophytes, 0.75 for sclerosis and 0.82 for vertebral narrowing, indicating good reproducibility for all features. Using the atlas, we have recently defined the descriptive epidemiology of the individual radiographic features of lumbar disc degeneration (LDD).[5] We have also shown strong associations between bone mass at the hip, osteophytes and end-plate sclerosis, although not disc space narrowing.[6]

Analysis

The association between individual radiographic features at each vertebral level (L1/2–L4/5) was assessed using Spearman's

Abbreviations: LDD, lumbar disc degeneration

Table 1 Correlations between the individual radiographic features by vertebral level

	Osteophytes				Sclerosis				Vertebral Narrowing			
	L1/2	L2/3	L3/4	L4/5	L1/2	L2/3	L3/4	L4/5	L1/2	L2/3	L3/4	L4/5
Osteophytes												
L1/2	–	–	–	–	–	–	–	–	–	–	–	–
L2/3	0.45*	–	–	–	–	–	–	–	–	–	–	–
L3/4	0.38*	0.59*	–	–	–	–	–	–	–	–	–	–
L4/5	0.27*	0.36*	0.45*	–	–	–	–	–	–	–	–	–
Sclerosis												
L1/2	0.51*	0.33*	0.28*	0.16*	–	–	–	–	–	–	–	–
L2/3	0.34*	0.53*	0.36*	0.20*	0.51*	–	–	–	–	–	–	–
L3/4	0.22*	0.38*	0.48*	0.26*	0.33*	0.50*	–	–	–	–	–	–
L4/5	0.19*	0.17*	0.20*	0.44*	0.23*	0.27*	0.36*	–	–	–	–	–
Vertebral narrowing												
L1/2	0.36*	0.17*	0.09	0.02	0.47*	0.34*	0.20*	0.21*	–	–	–	–
L2/3	0.24*	0.34*	0.18*	0.03	0.32*	0.48*	0.31*	0.19*	0.62*	–	–	–
L3/4	0.18*	0.28*	0.27*	0.08*	0.22*	0.35*	0.44*	0.22*	0.46*	0.66*	–	–
L4/5	0.17*	0.16*	0.15*	0.28*	0.16*	0.17*	0.21*	0.44*	0.34*	0.38*	0.53*	–

*$p<0.05$.

correlation coefficient. Log-linear modelling was then used to look at the strength of individual pairwise associations.

In the log-linear model, the outcome variable is the number of vertebrae with each possible combination of the three radiographic features, and the predictor variables are four-valued categorical variables (0–3) measuring the severity of each of the features. The basic log-linear model takes the form:

$\log(p_{ijk}) = \beta_i+\beta_j+\beta_k$

where p_{ijk} is the probability that a vertebra has a score of i for osteophytes, j for sclerosis and k for narrowing.

β_i, β_j and β_k are the corresponding regression coefficients.

The above model assumes that there is no association between any of the features. Associations between features can be modelled by including interaction terms, formed by multiplying the scores for two of the features together. For example, the interaction between narrowing and sclerosis measures the increasing frequency of sclerosis in vertebrae where narrowing is apparent. If the regression coefficient (β) for this interaction is significantly greater than 0, then sclerosis is more likely to occur where there is narrowing than where there is not. All two-way interactions (osteophytes+sclerosis, osteophytes+narrowing, sclerosis+narrowing) were fitted in the model.

Separate models were fitted for individual vertebral levels. A model was also fitted to the data from all four vertebral levels, stratifying by subject and vertebral level. As the observations were no longer independent when all four vertebral levels were included in the model, robust or ''sandwich'' estimators of standard errors were used when calculating confidence intervals (CIs), as they allow the possibility of correlations between the observations. The results of the analyses are expressed as β coefficients and 95% CI. Statistical analysis was performed using STATA v.6.0.

RESULTS

Subjects

In all, 286 men (mean age 65.3 years, standard deviation (SD) = 8.9) and 299 women (mean age 65.2 years, SD = 8.9) were included in the analysis. In total, 2340 individual vertebral levels were assessed. On the basis of a cut-off grade >0, 73.0% of vertebral levels had evidence of osteophytes, 25.6% sclerosis and 36.7% disc space narrowing.

Association between radiographic features by vertebral level

Table 1 shows the correlations between individual radiographic features at different vertebral levels. In general, the sizes of the correlation coefficients were greater between adjacent than between non-adjacent vertebra; thus, for example, for osteophytes, the correlation was greater between L2/3 and L3/4 (r = 0.59) than between L1/2 and L3/4 (r = 0.38) or between L2/3 and L4/5 (r = 0.36).

There were significant correlations also between radiographic features (table 1). These tended to be greater for osteophytes with sclerosis (range (L1/2–L4/5) 0.16–0.53) than for the other pairwise combinations. The size of the pairwise correlation coefficients tended to be greater at the same vertebral level and decreased with increasing distance between vertebra. Thus, for example, for sclerosis at L1/2, the correlation coefficients with osteophytes were greater at L1/2 (r = 0.51) than at the other vertebral levels, L2/3 (r = 0.33), L3/4 (r = 0.28) and L4/5 (r = 0.16).

Log-linear model

Table 2 shows the interaction terms between the individual radiographic features for all vertebrae and by vertebral level using the log-linear model. There were significant associations between all pairwise combinations of features. On the basis of the model which included all vertebral levels, the interaction was strongest for osteophytes and sclerosis (β coefficient = 2.7). The interaction was weakest, although still significant for osteophytes and narrowing (β coefficient = 1.2). In this model using formal testing, all interaction terms were significantly different from each other ($\chi^2 = 71.04$; $p = 0.001$). When the

Table 2 Interactions between the individual radiographic features of lumbar disc degeneration by vertebral level

Interaction	L1/2	L2/3	L3/4	L4/5	All
Osteophytes × sclerosis	2.7 (2.1 to 3.4)	2.9 (2.3 to 3.7)	2.4 (2 to 3)	3.1 (2.3 to 4.3)	2.7 (2.4 to 3.1)
Sclerosis × narrowing	2.2 (1.7 to 2.8)	2.0 (1.6 to 2.5)	2 (1.7 to 2.5)	2.3 (1.8 to 2.9)	1.9 (1.7 to 2.1)
Osteophytes × narrowing	1.3 (1.1 to 1.6)	1.2 (1 to 1.4)	1.2 (1 to 1.4)	1.2 (1 to 1.3)	1.2 (1.1 to 1.3)

Values are given as β coefficient (95% CI).

Table 3 Number of vertebra with each combination of individual radiographic features

Osteophyte	Sclerosis	Narrowing	Observed	Predicted*	Predicted†
0	3	0	0	3.8	0
0	3	1	0	1.5	0
0	3	2	0	0.4	0
1	3	2	0	0.8	0.2
0	2	3	0	1.1	0.2
0	2	2	0	1.8	0.2
2	3	0	0	2.2	0.2
0	2	0	0	15.9	0.4
2	3	1	0	0.9	0.6
2	3	2	0	0.3	0.9
3	0	3	0	5.3	1.1
3	3	1	0	0.4	2.1
1	3	0	1	6	−0.9
1	3	1	1	1.8	−0.9
1	3	3	1	−0.5	−0.7
0	2	1	1	5.3	−0.7
3	3	0	1	−0.1	−0.3
2	3	3	1	−0.8	1.1
0	3	3	2	−1.7	−2
0	1	3	2	3.9	0
1	2	3	2	0.1	1.3
3	3	2	2	−1.9	2
3	0	2	3	5.6	−0.4
0	1	2	3	6.7	1.4
1	2	1	4	7.7	0.8
2	2	0	4	5.3	2.1
3	1	3	4	−2.5	5.6
1	2	0	5	24.6	−0.8
2	0	3	5	7.5	−0.5
3	2	0	5	−1	1.4
1	2	2	6	−2.6	−2.7
3	2	1	7	−5.4	4
1	0	3	8	31.6	15.1
0	0	3	10	11.3	−5.1
2	2	2	10	−8.9	−2.8
3	1	2	10	−7.6	2
2	2	1	11	−7.3	−2.4
3	2	2	11	−10.5	0.3
1	1	3	12	−0.9	2.6
2	2	3	13	−12.3	−4.2
3	3	3	13	−12.9	−2.2
2	0	2	13	−7.2	−0.3
0	1	1	13	20	14.4
3	2	3	14	−13.7	2.7
1	1	2	15	3	12
3	0	1	17	12.4	−8.4
2	1	3	19	−15.5	−5
3	0	0	19	55.7	−1.8
3	1	1	21	−12.8	0.6
0	0	2	23	11.6	−2.8
0	1	0	23	60.8	25.2
2	1	2	28	−22.3	−6.8
3	1	0	32	−11.1	−8.7
1	0	2	48	16.3	−3.2
1	1	1	54	7.3	18.4
2	0	1	56	12.9	−4.5
2	1	0	63	−14.1	−1.6
2	1	1	67	−47.7	−20.4
2	0	0	82	92.8	43.4
0	0	1	114	4	7.8
1	1	0	123	32.6	−6.7
1	0	1	220	−0.9	1.5
0	0	0	446	−146.6	−5.9
1	0	0	683	−127	−26.1

*Difference between predicted and observed counts based on model with no interactions.
†Difference between predicted and observed counts based on model with interactions.

individual vertebral levels were considered, the results were broadly similar (table 2).

Table 3 shows the number of vertebra with each combination of scores of the individual radiographic features. The observed count is shown along with two predicted counts, one without the interactions between the radiographic features included and one with. The predicted count, which takes into account the pairwise interactions, was closer to the observed count. Including the interaction terms led to a statistically significant improvement in the model ($\chi^2 = 352.01$, $p<0.05$).

DISCUSSION

In this study, we found that increasing severity of all three radiographic features of LDD was associated with increasing

severity of the other features, although the association was strongest for osteophytes and end-plate sclerosis, and was stronger within than between vertebral levels.

There are some methodological limitations that need to be considered when interpreting the findings. The response rate for participation in the study was 61%.[7] Those who attended for screening could have differed with respect to the frequency of disc degeneration than those who did not attend. Given, however, that the analysis of the inter-relationships between radiographic features was based on an internal comparison of responders, non-participation bias is unlikely to have had a major effect on the observed findings.

The semiquantitative approach used here to characterise the individual radiographic features is subject to errors of precision. Formal assessment of intraobserver variability as determined by κ was good. At the time of assessment, the observer was not aware of any possible difference in pairwise associations between features and any errors in classification of the features likely to have been non-directional, and would tend to reduce the chance of finding true associations.

As with peripheral osteoarthritis, the pathogenesis of intervertebral disc degeneration remains poorly characterised. Degenerative changes within the disc may result in an alteration of its mechanical properties, increased flexibility and decreased disc height, which in turn contribute to changes in the local stress/strain state within the disc.[8] Also, as has been considered for peripheral osteoarthritis,[2] the bone may be the primary trigger responding to lifelong stress with hypertrophy and stiffening, and transmitting increased load to the intervertebral disc. In peripheral osteoarthritis, there is some evidence that increased bone mass is a predictor of radiographic osteoarthritis.[9 10] It has also been shown that generalised osteoarthritis is associated with increased levels of insulin-like growth factors in extracts of cortical bone from the iliac crest.[11]

If osteophytes and end-plate sclerosis are independent and separately related to narrowing of the disc, then we could hypothesise that as disc space narrowing increased, the severity of these features would increase in parallel. However, we observed that the proliferative features were more likely to be related in terms of severity than either separately with disc space narrowing.

There are few data concerning inter-relationships between component radiographic features of LDD in the literature. In a Japanese study, there were significant correlations between osteophytes, end-plate sclerosis and disc space narrowing in the lumbar spine, although data relating to these features were pooled rather than considered by vertebral level.[12] As in our study, the association between osteophytes and end-plate sclerosis was stronger (correlation coefficient 0.47) than either of the other pairwise correlations (correlation coefficients 0.34 and 0.38). In a study of twins using magnetic resonance imaging, a strong correlation was seen between the same measurements (including disc height and osteophytes) across all vertebral levels within the cervical and lumbar spine, but a weaker correlation when the same features were compared between the cervical and lumbar spine.[13]

In a series of paleopathological specimens,[1] it was observed that individuals who had a tendency to form enthesophytes were more likely to have both osteophytes and sclerosis present at peripheral joint sites. These data have been considered to be consistent with a bone proliferative response to disease occurrence.[2] Although the pathologies of disc degeneration and peripheral osteoarthritis are different, our data in relation to severity of osteophytes and sclerosis would be consistent with this. Further research is necessary to determine the factors affecting the occurrence and severity of these features.

We have previously shown in this population sample an association between radiographic features of disc degeneration and back pain although disc space narrowing was more strongly associated than the other features.[5] All three features increased in frequency with age.[5] We found evidence also of an association between bone mineral density at the femoral neck and the presence of vertebral osteophytes and end-plate sclerosis, although not disc space narrowing.[6] However, further prospective data are required both to confirm our findings and to determine the temporal nature of the observed associations.

In summary, the association between increasing severity of osteophytes and end-plate sclerosis is stronger than for other combinations of radiographic features of LDD.

ACKNOWLEDGEMENTS

We thank the Arthritis Research Campaign for their support.

Authors' affiliations

Stephen R Pye, Mark Lunt, Alan J Silman, Terence W O'Neill, arc Epidemiology Unit, The University of Manchester, Manchester, UK
David M Reid, Department of Medicine and Therapeutics, University of Aberdeen, Aberdeen, UK
Judith E Adams, Clinical Radiology, Imaging Science and Biomedical Engineering, The University of Manchester, Manchester, UK

Competing interests: None.

REFERENCES

1 **Rogers J**, Shepstone L, Dieppe P. Is osteoarthritis a systemic disorder of bone? *Arthritis Rheum* 2004;**50**:452–7.
2 **Felson DT**, Neogi T. Osteoarthritis: is it a disease of cartilage or of bone? *Arthritis Rheum* 2004;**50**:341–4.
3 **O'Neill TW**, Felsenberg D, Varlow J, *et al*. The prevalence of vertebral deformity in European men and women: The European Vertebral Osteoporosis Study. *J Bone Miner Res* 1996;**11**:1010–18.
4 **Garton MJ**, Abdalla MI, Reid DM, *et al*. Estimating the point accuracy of population registers using capture-recapture methods in Scotland. *J Epidemiol Commun Health* 1996;**50**:99–103.
5 **Pye SR**, Reid DM, Smith R, *et al*. Radiographic features of lumbar disc degeneration and self-reported back pain. *J Rheumatol* 2004;**31**:753–8.
6 **Pye SR**, Reid DM, Adams JE, *et al*. Radiographic features of lumbar disc degeneration and bone mineral density in men and women. *Ann Rheum Dis* 2006;**65**:234–8.
7 **O'Neill TW**, Marsden D, Matthis C, *et al*. Survey response rates: national and regional differences in a European multicentre study of vertebral osteoporosis. *J Epidemiol Commun Health* 1995;**49**:87–93.
8 **An HS**, Anderson PA, Haughton VM, *et al*. Introduction: disc degeneration: summary. *Spine* 2004;**29**:2677–8.
9 **Sowers M**, Zobel D, Weissfeld L, *et al*. Progression of osteoarthritis of the hand and metacarpal bone loss. A twenty year followup of incident cases. *Arthritis Rheum* 1991;**34**:36–42.
10 **Burger H**, van Daele PL, Odding E, *et al*. Association of radiographically evident osteoarthritis with higher bone mineral density and increased bone loss with age. *Arthritis Rheum* 1996;**39**:81–6.
11 **Dequeker J**, Mohan S, Finkelman RD, *et al*. Generalized osteoarthritis associated with increased insulin-like growth factor types I and II and transforming growth factor beta in cortical bone from the iliac crest. Possible mechanism of increased bone density and protection against osteoporosis. *Arthritis Rheum* 1993;**36**:1702–8.
12 **Muraki S**, Yamamota S, Ishibashi H, *et al*. Impact of degenerative spinal diseases on bone mineral density of the lumbar spine in elderly women. *Osteoporos Int* 2004;**15**:724–8.
13 **Sambrook PN**, MacGregor AJ, Spector TD. Genetic influences on cervical and lumbar disc degeneration. *Arthritis Rheum* 1999;**42**:366–72.