Osteophyte Volume Increases with Age and Caudal Vertebral Level in Individuals with Chronic Low Back Pain

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INTRODUCTION: Chronic low back pain (cLBP) is often accompanied by changes in bony morphology of the lumbar spine including spondylosis, sclerosis, narrowing of the intervertebral space, and osteophyte growth[1]. Previous work has indicated osteophyte severity increases at more caudal vertebral levels[2], while the prevalence remains similar across all vertebral levels[3,4]. Additionally, the prevalence of osteophytes has been seen to increase with age for both men and women [3,4]. However, all previous work evaluating osteophyte severity has been limited to subjective, categorical scoring[1-4], which can be unreliable. Additionally, to our knowledge, no work has been done to quantify the osteophyte volume in the lumbar spine. Therefore, the purpose of this study was to develop an automated method to calculate osteophyte volume in lumbar vertebrae, and to evaluate the relationships between osteophyte volume and vertebral level, age, and sex. Our hypotheses were: (1) osteophyte volume will increase with each more caudal vertebral level, (2) osteophyte volume will increase with age and (3) osteophyte volume would be larger in men than women.

METHODS: Written informed consent was obtained from individuals having cLBP (defined as low back pain for more than 3 months that persists >50% of the time in the last 6 months), with BMI <35 kg/m^2, who were not pregnant, and were able to perform lumbar flexion/extension and lateral bending. Lumbar spine CT scans were acquired in the supine position (resolution: 0.35x0.35mm in-plane, 0.625mm slice thickness). Bone tissue from L1 through S1 was segmented from the CT scans using a combination of automated and manual segmentation (Mimics 26, Materialise). Lumbar vertebrae 3D models were then created from the segmented bone tissue[5]. The vertebral body was separated from the posterior elements by identifying three points at the most anterior sections of the pedicles in Mimics and using a plane fit through those points to cut the model. A "healthy" library of 176 lumbar bone models were identified from previous studies[6-8] and participants under the age of 40 from this dataset, all who were evaluated as lacking osteophytes by a variety of reviewers (researchers and clinicians). Each bone from cLBP patients was then iteratively matched to every bone in the healthy library using Procrustes analysis adapted from the methods previously done in the CMC joint[9]. Bone volume of the best-fit healthy bone was then subtracted from each vertebra, leaving the osteophytes, where the volume was then calculated. 32 bone models with artificially generated osteophytes of known volume were run through the same algorithm to assess bias and accuracy (RMSE). One-way repeated measures ANOVA was used to evaluate differences between vertebrae within a subject in total osteophyte volume while linear regression was used to evaluate the changes in osteophyte volume with increasing caudal location. Multiple linear regression was used to evaluate associations between age, sex, and osteophyte volume at each vertebral level. Significance was set at $p < 0.05$ for all tests.

RESULTS: 264 of the 300 enrolled subjects were included in this analysis (average age: 56.7±15.9 years, 144F). The algorithm RMSE was 149.2mm^3, with a bias of -84.3mm^3. Osteophyte volume increased an average of 147.8mm^3 with each caudal vertebral level (Figure 1, B = 147.8, $p < 0.001$). L1 had significantly less osteophyte volume than all other bones (all $p < 0.001$), L5 had significantly more osteophyte volume than all other bones (all $p < 0.001$), and L2, L3, and L4 were not significantly different from each other (all $p > 0.07$). Multiple linear regression found both age and sex were significant predictors of osteophyte volume (all $p < 0.001$, $R^2 \geq 0.401$, Table 1). For every one-year increase in age, osteophyte volume increased between 34.3mm^3 at L1 to 47.7 mm^3 at L5 (Figure 2, Table 1, all $p < 0.001$). Men had between 948.6 and 1007.3mm^3 more osteophyte volume than women (Figure 2, Table 1, all $p < 0.001$).

Table 1. Multiple linear regression output for each vertebral level. Units for unstandardized beta are mm^3.

Regression Output		L1	L2	L3	L4	L5
R^2		0.401	0.486	0.481	0.465	0.443
Unstandardized Beta	Age	34.3	41.9	44.5	41.8	47.7
	Sex	-948.6	-948.5	-1007.3	-974.4	-983.1

DISCUSSION: These results suggest osteophyte volume increases with more caudal lumbar vertebrae in patients with cLBP, supporting our first hypothesis. Our results also show osteophyte volume increases with age, supporting our second hypothesis. While we did find osteophyte volume was associated with age and sex, our linear regression models only described about 45% of the variance in the data. This finding, in addition to the qualitative observation that the range in osteophyte volume was much larger after 60 years of age, suggests there may be additional factors that could help explain differences in osteophyte volume, specifically in patients >60 years. These results are limited to individuals with cLBP.

CLINICAL SIGNIFICANCE: Greater understanding of osteophyte formation in patients with cLBP may be valuable in clinicians' assessment and treatment of cLBP.

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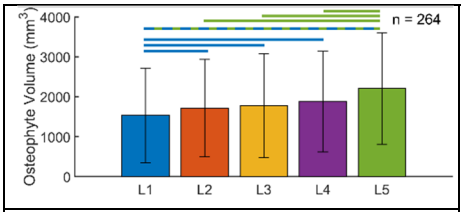

Figure 1. Average osteophyte volume at L1 (blue), L2 (red), L3 (yellow), L4 (purple) and L5 (green). Error bars indicate ±1SD. Colored bars indicate significant differences between levels.

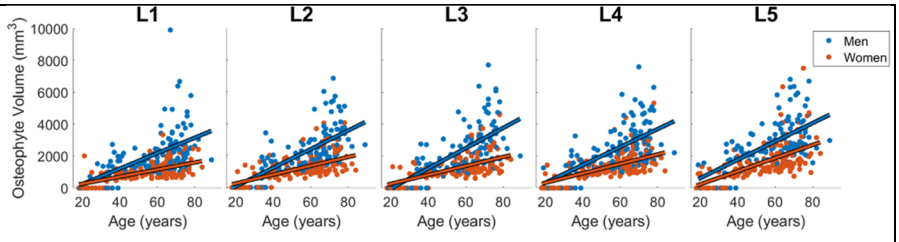

Figure 2. Osteophyte volume with age at each vertebral level. Men are plotted with blue dots while women are plotted in red.