

## EFFECT OF VITAMIN D THERAPY ON SYNOVIAL TISSUE VOLUME AND BONE MARROW LESIONS IN SYMPTOMATIC KNEE OSTEOARTHRITIS

**Purpose:** Vitamin D has biological effects on multiple knee joint structures and data from observational studies suggest vitamin D deficiency may be linked with pain and progression of knee OA. In the UK VIDEO study, a multicentre 3-year randomised placebo controlled trial of vitamin D therapy (800 IU/day) in patients with symptomatic knee OA, there was no evidence of an effect of vitamin D therapy on either pain or structural progression of disease as assessed using x-rays. We hypothesised, however, that there may be an effect of treatment on the occurrence of synovial tissue volume (STV) and bone marrow lesions (BMLs), as assessed by magnetic resonance imaging (MRI).

**Aim:** The aim of this analysis was to determine the effect of vitamin D therapy on synovial tissue volume and BML volume.

**Methods:** Data were collected on the sub-sample of symptomatic knee OA participants in the UK VIDEO study who obtained MRIs from the baseline visit. In the trial, patients recruited to one of five study sites (Southampton, UK) had assessment of MR imaging at yearly intervals. Subjects completed the WOMAC questionnaire which included questions about knee pain and function at baseline and at each follow-up. Semi-automated segmentation of enhancing STV and subchondral BMLs across the whole knee joint of the index knee was performed on sagittal T1-weighted fat-suppressed post-contrast scans using in-house, thresholding software. Subchondral BMLs were defined as ill-defined areas of hyperintensity on post-contrast images on  $\geq 2$  consecutive slices. To determine the impact of treatment on STV & subchondral BML volume, we used random-effects multiple linear panel regression modelling, adjusting for baseline values of the outcome, age and gender. We looked also at the association between structural outcomes and pain using a random-effects multiple linear panel regression, adjusting for variance between follow-up visits.

**Results:** 50 patients had contrast enhanced MR scans at baseline and a minimum of 1 follow-up MR scan during the first 24 months of study. Their mean age was 63.3 (SD  $\pm$  6.5) years and 74% were female. Intra-observer agreement for assessment of STV and BMLs was excellent (ICC (2,1) = 0.99 for both) and inter-observer agreement was very good (ICC (2,1) range = 0.83 to 0.99). After adjusting for age, gender and baseline value of the outcome, the adjusted mean difference in synovial tissue volume (STV) at 2 years follow-up between treatment groups was -611 mm<sup>3</sup> (95% CI -2208.9 to 986) and total subchondral BML volume was -111 mm<sup>3</sup> (95% CI -2961 to 2738) (table 1). A significant association was observed between STV and WOMAC pain score (b = 43.9 mm<sup>3</sup>; 95% CI 13.0 to 74.7), WOMAC function (b = 34.6 mm<sup>3</sup>; 95% CI 6.2 to 63.0), and WOMAC total score (b = 40.6 mm<sup>3</sup>; 95% CI 9.5 to 71.7). There were no significant associations between any of the WOMAC scores and BML volume.

**Conclusion:** Our data suggests that vitamin D therapy does not have an effect on synovial tissue volume or BMLs in symptomatic knee OA. Synovitis assessed using contrast enhanced MR scans, though not BMLs was associated with knee pain and function.

Table 1. Adjusted between-group mean differences in total synovial tissue volume (mm<sup>3</sup>) and total subchondral BML volume (mm<sup>3</sup>).

<i>Adjusted Mean Difference Between Treatment Groups. Mean (95% CI)<sup>a</sup>.</i>		
<i>Structural Parameters</i>	<i>Year 1</i>	<i>Year 2</i>
<b>Total Synovial Tissue volume (STV)</b>	-152.6 (-1605.2 to 1300.1)	-611 (-2208.9 to 986)
<b>Total Subchondral BML volume</b>	225.5 ( -2416.8 to 2867.8)	-111 (-2961 to 2738)

Abbreviations: BML, Bone Marrow Lesion; CI, Confidence Intervals.

<sup>a</sup> Adjusted mean differences between treatment groups at 12 and 24 months follow-up were generated from mixed effects models adjusted for; baseline STV (or total subchondral BML volume), age and gender.