FRI0301 ROLE OF VITAMIN D IN OSTEOARTHRITIS KNEE: A SIX MONTH DOUBLE BLIND, RANDOMIZED, PLACEBO CONTROL TRIAL

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Background: There is a putative role of vitamin D in osteoarthritis (OA) based on animal, epidemiological and human clinical studies. Short term clinical studies suggest beneficial influence of vitamin D on local changes in the bone which probably accounts for diminished pain experienced in knee OA (KOA)[1]. Inadequate sunlight exposure and lower serum levels of 25(OH)D appears to be associated with an increased risk for progression of OA knee[2]. Some chronic analgesic users with OA knee were more likely to be in lower categories of 25(OH) D compared to women with asymptomatic OA[3]
Objectives: A six month, double blind, randomized and placebo controlled trial of vitamin D, in vitamin D insufficient OA knee subjects (serum 25(OH)D levels <50 nmol/L) was conducted.
Methods: 150 subjects of primary OA knee, diagnosed by ACR guidelines, were subjected to personal interview to determine their vitamin D intake (by 3 day dietary recall and food frequency table) and the daily sunlight exposure in hours. Serum levels of calcium, phosphorus, alkaline phosphatase and 25(OH) D were measured to determine their vitamin D profile. We identified 64 vitamin D insufficient subjects out of 150 primary OA knee patients. These were randomized by random allocation table for intervention. In cases a bolus dose of calciferol in 60,000 IU/day for 10 days followed by 6,000 IU/month for six months was administered and in controls a placebo in the same schedules and durations was given. Primary outcome measures were clinical WOMAC scores (pain, stiffness and physical function) and VAS for knee pain. Secondary outcome measures were radiological features (joint space width, osteophyte scores, subchondral sclerosis scores and tibio femoral alignment) and KL grades. The serum levels of vitamin D were assessed by using Enzyme Linked Immunosorbent Assay (ELISA) and calcium/phosphorus/alkaline phosphatase by UV end point method. Statistical analysis was performed on an intension to treat basis.
Results: There was no significant baseline difference of age, sex, analgesic frequency, dietary vitamin D intake, serum levels of vitamin D, calcium, phosphorus and alkaline phosphatase and in clinical and radiological scores between the cases and controls. BMI (25.96 vs 25.65, p=0.75) and pain (10.94 vs 10.64, p=0.66) was higher in the placebo group although difference was not statistically significant. There was no significant difference in radiological features and KL grades from baseline and at 6 months in both the groups.
At six month, both the groups had an improvement in WOMAC and VAS pain scores but vitamin D showed benefit over placebo from baseline ($p<0.01$); for WOMAC physical function vitamin D group showed significant improvement over placebo which remained same as their baseline levels.
Conclusions: Although a long term study is being recommended to establish radiological progression, this short term randomized placebo control trial yields a beneficial effect of vitamin D in pain and physical function outcomes in KOA. Vitamin D intake was beneficial in symptomatic improvement of KOA
References:
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FRI0302 WORSENING OF HOFFA-SYNOVITIS AND EFFUSION-SYNOVITIS INCREASE RISK FOR TOTAL KNEE REPLACEMENT

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Background: Total knee joint replacement (TKR) is a cost-effective procedure with good long-term outcomes. However, at present there is no clear consensus on indications for TKR. Imaging biomarkers capable of predicting TKR therefore are urgently needed and may be helpful in clinical studies and trials which utilize TKR as an outcome. Hoffa-synovitis and effusion-synovitis, which may be assessed on non-contrast enhanced MRI, have been identified as important disease features relevant for clinical disease manifestations such as pain but may also be relevant for structural progression. Furthermore, worsening or improvement in these inflammatory imaging markers is associated with worsening or improvement in pain. For these reasons Hoffa- and effusion-synovitis are promising candidate imaging biomarkers for TKR.
Objectives: Aim of the study was to assess if presence or worsening of Hoffa- and effusion-synovitis prior to TKR increases risk for TKR and if change in these two measures prior to TKR further affects the risk for TKR.
Methods: We studied 121 knees from OAI participants (age 45-78 years) that underwent TKR before the 48 month visit using the time point prior to TKR, (e.g. for a TKR reported at the 48 month (M) visit, T0 =36M and T-1 =24M) and 121 control knees that did not undergo TKR that were matched for radiographic disease stage, gender, and age and were assessed at the same T0 and T-1 follow-up visit. Images were acquired at four OAI clinical centers using dedicated 3 T scanners. MRIs were read for Hoffa- and effusion-synovitis using the semiquantitative MOAKS system, which scores both features from 0-3 with 0 being normal and 3 coding severe structural changes. Conditional logistic regression comparing matched knees was applied to assess the risk of TKR at T0. In addition change in Hoffa- and effusion-synovitis from the time point prior (T-1) to T0 was analyzed in regard to risk for TKR following T0.
Results: Subjects were on average 65.5 years old (SD $\pm$ 8.6), predominantly female (58.1%) and overweight (mean BMI 29.5 SD $\pm$ 4.88). In the comparison of the T0 time point, the odds for TKR were significantly increased for the group exhibiting any effusion-synovitis at T0 when compared to the knees without effusion-synovitis at T0 as the reference (OR 2.45 95% confidence interval [CI] 1.22-4.95). No significant associations were found for presence of Hoffa-synovitis at T0 (OR 1.11, 95% CI 0.58-2.15).
Worsening of either Hoffa- and effusion-synovitis from T-1 to T0 was associated with increased odds for TKR (OR 7.0, 95% CI 1.59,30.80 and 2.27, 95% CI 1.11,4.62 respectively).
Conclusions: Presence of effusion-synovitis at the time point prior to TKR (T0) increases risk of TKR, while presence of Hoffa-synovitis does not. The latter finding is likely explained by the non-specific character of this imaging marker. Worsening of Hoffa- and effusion-synovitis from T-1 to T0 both increase risk for TKR. Presence and change of these imaging markers are important prognostic markers in regard to the structural progression of knee OA using TKR as the outcome measure.
Disclosure of Interest: A. Guermazi Shareholder of: Boston Imaging Core Lab (BICL),LLC., Consultant for: Facet Solutions, Genzyme, Novartis, Stryker,Merck Serono, F. Roemer Shareholder of: Boston Imaging Core Lab (BICL), LLC., Consultant for: Merck Serono, NIH, M. Hannon: None Declared, R. Boudreau: None Declared, D. Hunter Grant/Research support from: Australia Research Council Future Fellowship, Consultant for: DonJoy, NIH, Stryker, F. Eckstein Shareholder of: Chondrometrics, D. Hayashi: None Declared, Z. Wang: None Declared, C. K. Kwoh Consultant for: Novartis

FRI0303 DEGREE OF SYNOVITIS ON MRI IS CORRELATED WITH HISTOLOGICAL AND MACROSCOPIC FEATURES OF SYNOVIAL TISSUE INFLAMMATION IN KNEE OSTEOARTHRITIS

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Background: Synovitis is often present on MRI of OA knees and is an important determinant of pain.
Objectives: To evaluate the association between synovitis at contrast enhanced (CE) MRI with microscopic and macroscopic features of synovial tissue inflammation.
Methods: A total of 43 patients with symptomatic radiographic knee OA attending the rheumatology or orthopaedic outpatient clinic were included. 22 patients (mean age 61$\pm$7yrs, 73% women, mean BMI 30$\pm$5kg/mm^2) underwent arthroscopy of the knee and macroscopic features (neovascularization, villi, fibrin and hyperplasia) were scored (0-4). Furthermore, 15-20 synovial biopsies per knee were obtained. 21 patients (mean age 60$\pm$11yrs, 52% women, mean BMI 30$\pm$5kg/mm^2) underwent arthroplasty and synovial tissues were collected. After haematoxylin and eosin staining, samples were microscopically scored on features: synovial lining layer hyperplasia (0-3), activation of resident cells/stroma (0-3) and degree of inflammatory infiltrates (0-3). Mean total scores (0-9) and feature score (0-3) by 3 observers were used. Saggital and axial T1-weighted CE MRI images (3T) were used to semi quantitatively score synovitis at 11 sites (0-22) according to Guermazi et al. (Ann Rheum Dis 2011). Self reported pain was assessed by visual analogue scale (VAS, 0-100). For comparison between groups, independent t-test and Mann Witney test were used when appropriate. Pearson adjusted for age or spearman rho correlations were used to calculate correlations for all 43 patients. Statistics were calculated by SPSS 17.0.
Results: The mean (SD) synovitis score on MRI was 8.0$\pm$3.7, representing a mild synovitis, and was significantly different between patients in arthroscopy group (6.4$\pm$2.7) and in arthroplasty group (9.7$\pm$3.8). A mean (SD) histology score of 2.5$\pm$1.6 was seen, which also differed between groups (2.0$\pm$1.4 vs 3.0$\pm$1.7, respectively). Median (range) score of macroscopic features (0-4) were 2 (1-4) for neovascularization, 1 (0-3) for hyperplasia, 2 (0-4) for villi and 2 (0-3) for fibrin. Mean VAS pain was significantly lower in the arthroscopy than in the arthroplasty group (44.4$\pm$23.0 vs 61.4$\pm$14.5, respectively). Synovitis score on MRI correlated with microscopic total synovitis score [r=0.6, P=0.000] and separate features (lining layer [r=0.4, P=0.016], stroma [r=0.3, P=0.033]

FRI0302 Worsening of HOFFA-synovitis and effusion-synovitis increase risk for total knee replacement

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