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Osteoporosis

OP0294

DIFFERENTIAL INFLUENCE OF CO-MORBIDITIES ON SITE OF FRAGILITY FRACTURES

M. Dey^{1,2}, M. Bukhari³. ¹Institute of Ageing and Chronic Disease, University of Liverpool, Musculoskeletal Biology I, Liverpool, United Kingdom; ²Aintree University Hospital, Liverpool University Hospitals NHS Foundation Trust, Academic Rheumatology, Liverpool, United Kingdom; ³Royal Lancaster Infirmary, University Hospitals of Morecambe Bay NHS Foundation Trust, Rheumatology, Lancaster, United Kingdom

Background: Fragility fractures (FF) can occur at various sites of the skeleton, and are associated with multiple risk factors [1]. The prevalence of FF markedly increases with age. As the longevity of the population increases, so will the incidence of FF, and that of associated co-morbidities and risk factors. There are few data on co-morbidities associated with fractures at each site.

Objectives: Identify associations of co-morbidities with sites of FF, by applying cluster analysis.

Methods: We reviewed 28868 patients presenting for BMD estimation at a district general hospital in North West England, 2004-2016. We identified patients who had sustained one or more FF at time of presentation. Site(s) of FF were recorded for each patient, including femur, forearm, humerus, pelvis, ribs, spine, tibia or fibula. The following co-morbidities or treatments were recorded: excess alcohol consumption (previous or current); bisphosphonates; coeliac disease; family history of FF; hormone replacement therapy; hyperparathyroidism; hyperthyroidism; inflammatory bowel disease; polymyalgia rheumatica; rheumatoid arthritis; smoking (previous or current); corticosteroids (previous or current). Cluster analysis was performed on fracture sites and co-morbidities, using Jaccard similarity coefficient, and plotted on a dendrogram. Results were divided into an optimal number of clusters, derived using the elbow and silhouette methods.

Results: 11003 of 28868 patients had sustained one or more FF at time of BMD estimation. Overall, 84.6% patients were female, mean age 67.5 years, and median T-score -1.12 SD. Cluster analysis was performed for FF sites and co-morbidities, with Jaccard similarity coefficients calculated. 4 clusters were identified (Figure 1): FF of forearm (n=5054), tibia/fibula (n=2617), spine (n=2352), associated with family history of FF, smoking, corticosteroids, and bisphosphonate treatment; FF of pelvis (n=300) associated with hyperparathyroidism, PMR, coeliac disease, and HRT; FF of femur (n=1181) and humerus (n=1131) associated with IBD and RA; FF of ribs (n=1022) associated with alcohol and hyperthyroidism.

Conclusion: Cluster analysis demonstrated 4 distinct subgroups of FF sites and associated co-morbidities. To our knowledge, this is the first study applying cluster analysis to evaluate co-morbidities associated with FF sites. Risk factors may influence trabecular more than cortical bone, accounting for the difference in clusters. Knowledge of risk factors associated with FF site subgroups will aid prophylaxis and management in at-risk patients.

References:

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Figure 1: Dendrogram of cluster analysis of 11003 patients with one or more fragility fractures. Fracture sites and co-morbidities/treatments are included. Optimal number of clusters was calculated using "Elbow method" and "Silhouette method." Clusters are defined by colour and grey dashed boxes. FH= family history; TibFib= fracture of tibia or fibula; Hyperparathyroid= hyperparathyroidism; PMR= polymyalgia rheumatica; Coeliac= coeliac disease; HRT= hormone replacement therapy; IBD= inflammatory bowel disease; RA= rheumatoid arthritis; Hyperthyroid= hyperthyroidism.

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OP0295

CORRELATION BETWEEN CORTICAL THICKNESS RELATIVE TO TRANSVERSE DIAMETER ON MID-PORTION OF THIRD METACARPAL BONE AND BONE MINERAL DENSITY IN LUMBAR SPINE AND FEMORAL NECK FOR PATIENTS WITH RHEUMATOID ARTHRITIS

I. Yoshii¹. ¹Yoshii Hospital, Department of Rheumatology and Musculoskeletal Medicine, Shimanto City, Japan

Background: Rheumatoid arthritis (RA) is a determinant risk factor of osteoporosis. BMD is clearly defined as diagnosis criteria of osteoporosis in Japan; that is less than -2.5 with T-score measured with dual-energy X-ray absorptiometry (DXA). The marker of T-score <-2.5 is widely used worldwide; however, the testing system is very expensive, preventing its extensive adoption.

Objectives: We tried to evaluate BMD not measuring with DXA, but the other method that substituting DXA with another X-ray picture of hand that is routinely taken for Sharp/van der Heijde score (SHS) calculation.

Methods: Patient with RA, who met the American College of Rheumatology/European League Against Rheumatism classification criteria, visited our institute has been routinely calculated SHS in taking X-ray pictures of bilateral hands and feet at first consultation. Cortical thickness was calculated from mid-portion of third metacarpal bone in X-ray picture that was taken for the calculation of SHS as taking cancellous bone diameter of the third metacarpal bone from transverse diameter at the same point. We set Cortical Thickness Ratio (CTR) as cortical thickness relative to transverse thickness (Figure 1). BMD measurements at the lumbar spine (LS) and femoral neck (FN) were obtained, and BMD values are presented as g/cm² and T-score showing dissociation of the BMD compared with the mean BMD in healthy 30-year-old of the same sex with standard deviation was also presented. Patient with RA who underwent SHS calculation and BMD measurement at first consultation was picked up for the study. Relationship between BMD and the other parameters such as sex (male/female), age, disease duration (years), ACPA titer, RF titer, body mass index (BMI), CTR, the HAQ score, DAS28-CRP, SHS, PS-VAS, tartrate-resistant acid phosphatase-5b value (TRACP-5b), previous treatment for osteoporosis and RA before initial consultation (pTx_OP and pTx_RA) (Yes/No) at initial consultation was evaluated with linear regression analysis.

T-score<-2.5 was statistically evaluated with binary regression analysis for the parameters that demonstrated significant correlation in multivariate linear regression analysis.

Then, Cut-off index (COI) of CTR for the BMD represented with T-score <-2.5 for both of LS and FN was evaluated with Receiver's Operation Characteristics technique (ROC). Sensitivity, specificity, area under curve, odds ratio with 95% confidence interval (95%CI) for T-score <-2.5 was also calculated.

Results: A total of 300 patients were picked up for the study. BMDs were 0.867 and 0.682 with 0.203 and 0.143 for standard deviations, that means T-score was -1.93 and -1.86 with 1.64 and 1.15 for standard deviations in LS and FN, respectively. Mean transverse width of third metacarpal bone was 7.3 mm and thickness of the cortex was 2.00 mm, so CTR was 0.279 in average and 0.124 for standard deviation.

In linear regression analysis, BMD in LS demonstrated significant correlation with sex, CTR, and DAS28-CRP, while BMD in FN demonstrated significant correlation with sex, age, and CTR.

In binary regression analysis, CTR and DAS28-CRP demonstrated significant positive correlation with T-score <-2.5 in LS, while age and CTR demonstrated significant correlation in FN.

In ROC, cut-off index of CTR was 0.25 in both of LS and FN, and sensitivities demonstrated 67.9% and 76.1%, and specificity demonstrated 83.0% and 81.6% in LS and FN, respectively. Area under curve was 0.78 and 0.81 with 4.17 (95%CI: 2.51 – 6.92) and 4.90 (95%CI: 2.75 – 8.73) of odds ratios for LS and FN, respectively (Figure 2).

Conclusion: Results of this cross-sectional study encourages our hypothesis that thickness of cortical bone relative to full thickness in the long bone reflects BMD. CTR correlated with BMD in both of LS and FN. CTR of third metacarpal bone was suggested that has close correlation with BMD in both LS and FN. CTR could be strong candidate marker for screening of osteoporosis in patient with RA with the index less than 0.25.

Figure 1: Calculation of CTR

Figure 2-a: LS

Figure 2-b: FN

X: COI; CTR < 0.25 for T-score < -2.5						
	Sensitivity	Specificity	AUC	odds ratio	95%CI	p-value
LS	67.90%	83.00%	0.78	4.17	2.51 - 6.92	3.43x10 ⁻⁸
FN	76.10%	81.60%	0.81	4.90	2.75 - 8.73	6.90x10 ⁻⁸

Figure 2-c: Sensitivity, Specificity, odds ratio, 95%CI, and p-value

Figure 2: Area under curve graph and statistics of cut-off index for LS and FN

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OP0296

SUPERIOR EFFICACY OF CALCIFEDIOL SOFT GELATIN CAPSULES VS CHOLECALCIFEROL FOR THE MANAGEMENT OF VITAMIN D DEFICIENCY IN POSTMENOPAUSAL WOMEN: A TREATMENT TO BE CONSIDERED IN THERAPEUTIC GUIDELINES

J. Del Pino^{1,2}, J. L. Pérez-Castrillón^{3,4}, A. Dueñas-Laita^{4,5}, G. Hernández⁶, P. Arranz-Gutiérrez⁶, S. P. Chinchilla^{7,8}. ¹Hospital Universitario de Salamanca, Salamanca, Spain; ²Universidad de Salamanca, Salamanca, Spain; ³Hospital Universitario Río Hortega, Internal Medicine, Valladolid, Spain; ⁴Universidad de Valladolid, Valladolid, Spain; ⁵Hospital Universitario Río Hortega, Clinical Toxicology Unit, Valladolid, Spain; ⁶Faes Farma, R&D and Innovation Department, Leioa, Spain; ⁷Faes Farma, R&D and Innovation Department, Leioa, Spain; ⁸University of the Basque Country (UPV/EHU), Leioa, Spain

Background: Vitamin D deficiency is a highly prevalent entity worldwide, with relevance in specific diseases and stages of life¹. Few guidelines assess the indications and optimal dosing in the general population, and although there is no international consensus, 800IU/day is associated with benefits in bone metabolism. Calcifediol, a vitamin D analog, is presented as a therapeutic alternative.

Objectives: To assess the efficacy of calcifediol in the treatment of vitamin D deficiency, compared with therapeutic guidelines recommendations for cholecalciferol in postmenopausal women.

Methods: Phase III-IV, double blind, randomised, controlled, multicentre superiority clinical trial. Postmenopausal women with baseline levels of 25(OH)D < 20ng/mL were randomised to three arms: 266 mcg of calcifediol/month for 4 or 12 months (standard and test regime), or to cholecalciferol 25000 IU/month for 12 months (as per therapeutic guidelines).

Results from an interim analysis - performed upon completion of month 4 visit by 100% of evaluable patients - are presented and reported without unblinding the study treatments. Both calcifediol groups are summarised for analysis.

The trial has been approved by the corresponding ethics committees and national competent authorities.

Results: 298 women were included in the ITT analysis. The average age was 63.4 ± 8.2 years, mean BMI was 29.3 ± 6 Kg/m², 10.7% had osteoporosis and received treatment. All demographic characteristics and risk factors for osteoporosis were balanced amongst groups.

When analysing per treatment group, 13.5% and 35% of women in the calcifediol group reached values of 25(OH)D > 30ng/mL at 1 and 4 months when compared to 0% and 8.2% respectively in the cholecalciferol group (p<0.01), achieving target levels in a rapid manner (Figure 1).

Figure 1. Regarding baseline levels, 25% of the population had levels <10ng/mL; in this group there were no statistically significant differences between both treatments, possibly due to the limited sample size. In the group with baseline levels from 10 to <20ng/mL, a statistically significant mean difference was observed at months 1 and 4, with a greater proportion of patients achieving both therapeutic levels in the calcifediol group (Table 1). No relevant safety issues were reported for the present analysis.

Table 1.

		Basal 25(OH)D levels			
		< 10ng/mL ^{NS}		10 to <20ng/mL ^{**}	
		Calcifediol (n= 54)	Cholecalciferol (n= 20)	Calcifediol (n= 146)	Cholecalciferol (n= 78)
Month 1	>30ng/mL	2 (3.7%)	0 (0%)	25 (17.1%)	0 (0%)
	>20ng/mL	12 (22.2%)	2 (10%)	106 (72.6%)	31 (39.7%)
Month 4	>30ng/mL	8 (14.8%)	1 (5%)	62 (42.5%)	7 (9%)
	>20ng/mL	27 (50%)	8 (40%)	135 (92.5%)	63 (80.8%)

^{NS}p>0.05; ^{**}p≤0.01

Conclusion: Calcifediol shows a greater efficacy than cholecalciferol regime (as recommended in therapeutic guidelines), for the treatment of vitamin D deficiency in postmenopausal women and in a timely manner, which could impact osteoporosis treatment. Cholecalciferol fails to achieve recommended levels in a significant proportion of this population. Baseline vitamin D levels are to be considered for the supplementation of vitamin D.

References:

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