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AB1323 OSTEOPHYTOSIS PROCESS SUGGEST INVOLVEMENT OF MAST CELLS, REVEALED BY WHOLE TRANSCRIPTOME ANALYSIS OF OSTEOPHYTES FROM KNEE OSTEOARTHRITIS PATIENTS

Priya Kulkarni¹, Sulev Koks¹, Abhay Harsulkar², Aare Martson³. ¹University of Tartu, Department of Pathophysiology, Tartu, Estonia; ²Bharati Vidyapeeth University, Department of Pharmaceutical Biotechnology, Pune, India; ³University of Tartu, Department of Traumatology and Orthopedics, Tartu, Estonia

Background: Cartilage-loss is a central pathology of osteoarthritis while synovitis, sub-chondral bone sclerosis and osteophytes (OFs) formation are counted as integral phenomenon. Osteophytosis is a process of OFs formation, in which mesenchymal stem cells from periosteum and synovium, along with a number of cytokines, growth factors and biochemical factors gives out bony out-growth at margin of the affected joint. Although frequently associated, OFs are one of the less focused areas in OA research, particularly from the molecular mechanism point of view, involved in their formation. Also, it is a good ambiguity if OFs is a pathological condition linked with altered biochemical milieu or a functional adaptation for the joint instability.

Objectives: Accounting its importance in clinical OA and the obscure biochemical background, this study strives for a deeper comprehension of molecular mechanism and active pathways, involved in OF formation

Methods: We performed whole transcriptome analysis of OFs, collected from six knee OA patients during knee replacement surgery. Non-OF tissue from tibial plateau of the same patient was used as a control. After RNA isolation, RNA-seq was performed using SOLiD 5500W platform and fragment sequencing chemistry. For differential gene expression analysis, non-normalized raw counts were used for the EdgeR package. To find differential transcriptome between OF and control, we used group-wise comparisons where negative binomial fitting was followed by exact test. Finally, RT-PCR of significantly expressed genes was run for transcriptome validation.

Results: After cluster analysis, total 597 genes were significantly expressed between OFs and controls out of which, 323 genes were seen up-regulated ($\text{LogFC} \geq 2$) while 274 were down-regulated ($\text{LogFC} \leq -2$). Further, 88 genes showed marked increase ($P < 0.01$); here CPA3, Selectin E, MS4A2, PLA2G2A and CSN1S1 were prominent. Similarly, 23 genes were with a noteworthy down-regulation ($P < 0.01$) and APOB, CADM2, TNEFF2, GNAZ and GABRA2 remained as first five. GO analysis of the best extracted genes indicated significant involvement of ECM proteoglycan, GABA A receptor pathway (Reactome 2016 - homo sapiens_R-HSA-3000178 and R-HSA-977441, respectively), osteoblast and TNF- α signalling pathways (WikiPathways 2016 -homo sapiens WP322 and homo sapiens WP231 respectively). Finally, transcriptome results were validated using RT-PCR of significantly expressed genes (CPA3, MMP-1, 3 and 13).

Conclusion: Significant expression of CXCL9, 10, 11 and PGR4 indicate chemotaxis and immune cells deployment; outstanding CPA3 and MS4A2

indicate active involvement of mast cells. Accounting a previous knowledge that 'mast cell products' are linked with increased osteoblastic and osteoclastic activity and impose pathological changes in articular and peri-articular tissue, marked expressions of MC products or mediators here, enable us to propose an association between MCs and OF. Presence of E-selectin on endothelial cell surface is known to promote adhesion of neutrophils and further release of TNF α and IL1. Expression of PLA2G2A suggests increased prostaglandin synthesis and indicates activation of inflammatory cascade. In conclusion, this transcriptome analysis suggests a significant association of mast cells with osteophytosis. The genes involving chemotaxis, degranulation, cytokinin synthesis mark the initiation of OF. On the other hand, proteases matrixremodelling enzymes may indicate their growth. A host of different signalling molecules denotes involvement of canonical and non-cannonical pathways that warrants further investigations.

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AB1324 MEASUREMENT PROPERTIES OF THE 10-ITEM CONNOR-DAVIDSON RESILIENCE SCALE AMONG PATIENTS WITH TOTAL KNEE REPLACEMENT BASED ON ITEM RESPONSE THEORY

Ka Keat Lim¹, Yu Heng Kwan¹, Seng Jin Yeo², William Yeo³, Julian Thumboo^{4,5}, David Matchar^{1,6}, Ying Ying Leung^{4,5}. ¹Duke-NUS Medical School, Programme in Health Services and Systems Research, Singapore, Singapore; ²Singapore General Hospital, Department of Orthopaedic Surgery, Singapore, Singapore; ³Singapore General Hospital, Orthopaedic Diagnostic Centre, Department of Orthopaedic Surgery, Singapore, Singapore; ⁴Singapore General Hospital, Department of Rheumatology and Immunology, Singapore, Singapore; ⁵Duke-NUS Medical School, Singapore, Singapore; ⁶Duke University Medical Center, Department of Medicine (General Internal Medicine), Durham, United States of America

Background: The number of older adults undergoing total knee arthroplasty (TKR) for knee osteoarthritis (OA) has been increasing. While psychological resilience may have a role in outcomes after TKR[1], no psychological resilience scale has been validated among patients with knee OA.

Objectives: To examine the measurement properties of the 10-item Connor-Davidson Resilience Scale (CD-RISC10) among older adults with knee OA.

Methods: Using data from 700 consecutive consented patients with knee OA enlisted for TKR, we examined four measurement properties of CD-RISC10. For **structural validity**, we fitted graded response model (grm) and examined standardized root-mean square residual (SRMR) for unidimensionality, Chi-square p-value for item fit, residual correlation for local independence and item-characteristic curves for monotonicity. For **internal consistency**, we examined Cronbach's alpha. For **construct validity**, we hypothesized that CD-RISC10 as a measure of psychological resilience would be moderately correlated (Pearson's R 0.30-0.50) with self-efficacy and mental well-being but weakly correlated (Pearson's R<0.30) with physical and social well-being (Table 1). For **measurement invariance**, we examined uniform and non-uniform differential item functioning (DIF) between gender, age group ($\leq$ median 66 vs >66 years), and language (English vs Chinese) and reported the McFadden's R². We used mirt and lordif packages on Rv64 v3.5.1 to examine grm and DIF respectively. We reported the findings based on COSMIN based Standards for the selection of health Measurement Instruments (COSMIN)[2].

Results: Of the 700 patients (age 65.5 $\pm$ 6.9 years old), 70.6% were females, 83.9% Chinese, 55% responded questionnaire in Chinese. Mean CD-RISC10 score was 27.5 $\pm$ 5.2, with minimal floor (0.1%) and ceiling effects (3.9%). CD-RISC10 demonstrated unidimensionality (SRMR=0.053), local independence (residual correlation=-0.025), monotonicity (adequate looking item characteristic curves) and internal consistency (Cronbach's alpha=0.91). Items 1 and 4 had potential misfit (Chi-square p>0.01). All a-priori hypotheses were met (Table 1). No item had significant DIF with age, gender and language, except item 4 had borderline non-uniform DIF across language (McFadden's R²=0.03).

Conclusion: We demonstrated structure validity, internal consistency, construct validity and measurement invariance of CD-RISC10 in the measurement of psychological resilience among older adults with knee OA.

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