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Systemic Biomarker for Early Diagnosis of Knee OA: A Systematic Review and Meta-Analysis

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INTRODUCTION:

Osteoarthritis(OA) is a complex progressive joint disorder, associated with synovium inflammation, joint cartilage degradation, subchondral sclerosis, and osteophyte formation. It is irreversible, so, it is crucial to diagnose it non-invasively at the earliest detectable stage. Various blood biomarkers(BMs) for knee OA(KOA) have been reported, however, there is no BM that diagnoses early KOA(eKOA), clinically and non-invasively, due to contradicting findings in the literature[1]. This systematic review and meta-analysis aimed to provide a structured review and meta-analysis of the current literature on early BMs detectable in circulation for eKOA.

MATERIALS & METHODS:

A structured search strategy was applied to search for original research articles on human studies of blood BMs for eKOA, based on Kellgren Lawrence(KL) grading[2], in three databases: Pubmed, SCOPUS and Web of Science. Only research studies with healthy control and eKOA groups(KL1/KL2) were selected. BMs were considered significant if reported with a fold change higher than 2 (for comparison between the eKOA group versus the healthy control group) and with $p<0.05$.

RESULTS AND DISCUSSIONS

A total of 110 articles fulfilled the inclusion and exclusion criteria and were included in this review and meta-analysis. We summarized several inflammation-related BMs(cytokines and chemokines) that have been reported as eKOA BMs: IL-1Ra, IL-6, IL-4, IL-15, IL-17, TNF-α, CXCL12 and calprotectine. Both CRP and ESR were also reported as significantly up-regulated in the eOA group. The reported BM related to cartilage/bone alterations for eOA were osteopontin**,** matrix MMPs, PIICP, fibulin-3, and dickkopf-1.

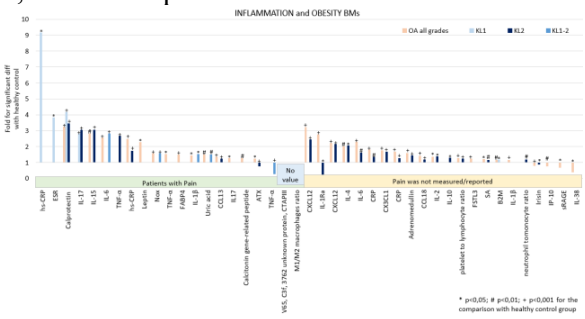

Figure 1: Inflammation and obesity related eKOA BMs.

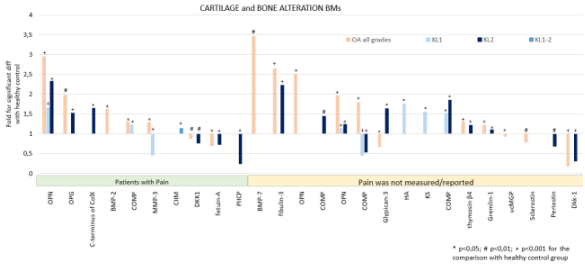

Figure 2: Cartilage/bone alteration related eKOA BMs.

CONCLUSION:

A total of 15 promising candidate eKOA blood BMs were identified. However, the evidence about their clinical effectiveness is still limited or reported with conflicting findings. More empirical studies with appropriate baseline control groups, are needed to provide more substantiated evidence to support the use of these BMs for clinical diagnosis of eKOA.

REFERENCES:

1. Im GI. *Tissue Eng Regen Med.* 2022.
2. Kellgren et al. *Ann Rheum Dis. 1957.*