

Ability of a Urine Assay of Type II Collagen Cleavage by Collagenases to Detect Early Onset and Progression of Articular Cartilage Degeneration: Results from a Population-based Cohort Study

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Abstract

Objective To evaluate the association of a sandwich assay for cartilage collagenase-mediated degradation, the C2C human urine sandwich assay (IB-C2C-HUSA), with early and late knee cartilage pathology and with progression of cartilage damage.

Methods A population-based cohort with knee pain, age 40–79 years, was evaluated at baseline ($n = 253$) and after mean 3.3 years ($n = 161$). We evaluated the IB-C2C-HUSA and a related competitive inhibition assay (C2C). The C2C assay was applied to serum (sC2C) and urine (uC2C). Based on knee radiographs and magnetic resonance imaging (MRI), 3 subgroups [no cartilage pathology, preradiographic cartilage pathology, and radiographic osteoarthritis (ROA)] were evaluated cross-sectionally for association with biomarker levels. Longitudinally, we evaluated whether baseline assays predict subsequent progression of cartilage degeneration, defined by MRI cartilage loss.

Results Cross-sectionally, statistically significant differences were seen in the 3 subgroups for IB-C2C-HUSA ($p < 0.001$), with the highest levels seen in ROA, and for sC2C ($p = 0.023$), while no differences were seen for uC2C ($p = 0.501$). Baseline IB-C2C-HUSA levels were higher in progressors vs nonprogressors ($p = 0.003$). In logistic regression analysis, only baseline IB-C2C-HUSA was associated with an increased risk of progression of cartilage damage (OR 1.78, 95% CI 1.03–3.09).

Conclusion The IB-C2C-HUSA degradation assay detects the generation of a pathology-related cartilage collagen peptide(s) that increase(s) with onset of degeneration of knee articular cartilage. The baseline values are associated with progression of cartilage degeneration over 3 subsequent years. This assay may have value in clinical OA trials. Further, it points to collagenase activity as a therapeutic target for controlling degeneration of articular cartilage.

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