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THE RELATION BETWEEN SERUM COMP AND CILP CONCENTRATIONS AND MRI SUBREGIONAL CARTILAGE THICKNESS CHANGE OVER THE FIRST FIVE YEARS AFTER ACUTE ACL INJURY - DATA FROM THE KANON-TRIAL

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Abstract:

Purpose:In parallel abstracts, we report serum concentrations of Cartilage Oligomeric Matrix Protein (COMP) and Cartilage Intermediate Layer Protein (CILP) as well as MRI derived subregional changes in cartilage thickness over 2 and 5 years after ACL injury in the KANON cohort. The purpose of this study was to relate change in MRI cartilage thickness and the two above molecular serum biomarkers of cartilage remodeling.

Methods:121 young active adults with an acute ACL tear were studied as part of the KANON randomized controlled trial. Sagittal MRIs (3D/WATSc) and serum samples were obtained within 5 weeks of the tear (BL), at Y2 and at Y5 follow-up; 107 (81 men, 26 women; median age 25.6y; age range 18-36) had complete series of MR images. Subregional cartilage thickness was analyzed in 16 femorotibial subregions and change between BL and Y2 and between Y2 and Y5 was summarized by computing a cartilage thinning score (summarizing all negative subregion changes) and a cartilage thickening score (summarizing all positive subregion changes) in each knee, regardless of location. A total subregional femorotibial cartilage change score was also computed by summarizing magnitudes of all subregional changes, independent of their direction. Serum concentrations of biomarkers were measured with a commercially available COMP sandwich ELISA (AnaMar AB) and an in-house research competitive inhibition assay for CILP (AnaMar AB). The relation between subregional MRI changes and serum biomarker concentrations was tested using the Spearman correlation coefficient; no correction for multiple testing was made in this exploratory analysis.

Results:Higher BL serum COMP concentrations predicted greater cartilage thickening ($r=0.22$, $p=0.025$) and thinning ($r=0.27$, $p=0.006$) over the first two years after acute ACL injury. BL serum COMP or CILP concentrations were not correlated to change in subregional cartilage thickness for any other investigated time period (Table 1). There were no significant associations between concurrent change of COMP or CILP serum concentrations and subregional cartilage thickness change between BL and Y2 ($-0.11 \leq r \leq 0.19$) or between Y2 and Y5 ($-0.03 \leq r \leq 0.08$). However, greater overall subregional cartilage thickness change between BL and Y2 predicted a decrease in serum COMP concentrations between Y2 and Y5 ($r=-0.23$, $p=0.017$). This was driven by a significant association between subregional cartilage thickening between BL and Y2 and serum COMP change between Y2 and Y5 ($r=-0.28$, $p=0.004$). No other significant associations were found between subregional cartilage thinning and serum COMP or CILP changes (Table 1).

Conclusions:Our results are the first to report on longitudinal associations between serum biomarkers and subsequent MRI cartilage changes in the ACL injured knee. Higher serum COMP concentrations within 5 weeks of acute ACL injury predicted both cartilage thickening and thinning over the first 2 years after ACL injury. Further, increased cartilage thickening over the first 2 years after injury predicted a decrease in serum COMP concentrations between Y2→Y5. Continued follow-up of this cohort and further biomarker analyses may clarify the relationship between early cartilage matrix changes, cartilage structure, and risk of later development of osteoarthritis.

Table 1. The correlation between serum COMP and CILP concentrations and cartilage thickness change as visualized on MRI over 5 years after ACL injury.

	Cartilage thickness change score		Cartilage thickening score		Cartilage thinning score	
	BL→Y2	Y2→Y5	BL→Y2	Y2→Y5	BL→Y2	Y2→Y5
COMP						
at BL	0.142	0.012	0.216*	-0.039	0.265**	-0.056
change 2Y – BL	0.074	0.034	0.002	-0.037	-0.111	-0.005
change 5Y – 2Y	0.232*	-0.126	-0.280**	-0.025	-0.073	-0.001
CILP						
at BL	0.066	-0.006	0.028	0.012	-0.019	0.030
change 2Y – BL	0.003	-0.015	0.186	-0.104	0.086	-0.144
change 5Y – 2Y	-0.003	0.008	-0.179	0.030	-0.156	0.081

Spearman correlations. * p<0.05; ** p<0.01

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