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SUBREGIONAL KNEE CARTILAGE THINNING OR THICKENING IS AGE- DEPENDENT AND IS ASSOCIATED WITH SERUM BIOMARKERS IN ADOLESCENT AND MATURE VOLLEYBALL ATHLETES

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Abstract:

Purpose: Cartilage structural change caused by aging, training or disease can be accurately and directly measured using MRI; while biomarker quantification from serum may be helpful in characterizing or predicting cartilage maturation. Cartilage Oligomeric Matrix Protein (COMP) represents an established serum biomarker of cartilage turnover, whereas Cartilage Intermediate Layer Protein (CILP) is a novel biomarker that is thought to be associated with cartilage degradation. In the current study we investigated whether MRI-based cartilage thinning and thickening in young and mature athletes is related to baseline or concurrent change in COMP and CILP levels.

Methods: Twenty adolescent (baseline age 16.0±0.6y) and 20 mature (46.3±4.7y) volleyball athletes were studied (10 men, 10 women). MR images (3D VIBE) and serum markers were obtained at baseline (BL) and at 2 year follow-up (Y2). Cartilage thickness was measured in 16 femorotibial subregions (8 medial, 8 lateral, 10 tibial, 6 femoral). Femorotibial subregional cartilage thinning (ThCTnS) and thickening (ThCTkS) scores were computed, by summarizing in each subject the BL→Y2 changes across all subregions with thinning and thickening, respectively. Further, a cartilage change score (ThCChS) was computed by summarizing the magnitudes of all subregional changes, independent of direction. COMP was analyzed using the commercial sandwich COMP ELISA (AnaMar AB) and CILP with an in-house research competitive immunoassay (AnaMar AB). Unpaired t-tests were used to compare results between female and male participants, paired t-tests to test whether change from BL→Y2 was significant, and linear regression to analyze the correlation between serum and imaging markers.

Results: Data on COMP and MRI was available in 18 mature (9 men, 9 women) and 12 adolescent athletes (9 men, 3 women); data on CILP and MRI was available in 15 mature (7 men, 8 women) and 8 adolescent athletes (6 men, 2 women) (Table 1). There was no indication of significant differences (defined by p≤0.05) in serum or imaging markers between men and women in mature (p>0.31) or adolescent athletes (p>0.17).

The mature athletes displayed much higher subregional cartilage thinning than thickening scores, and the adolescent athletes much higher thickening than thinning scores, whereas the non-directional change scores were similar in mature and adolescent participants (Table 1).

Pooled analyses in both sexes suggested a significant increase in CILP (p=0.02) for BL→Y2 in mature athletes, but no significant change in COMP (p=0.63). Similar relationships were observed in adolescent athletes (p=0.009 for CILP, and 0.88 for COMP).

In mature adults, BL→Y2 COMP change was negatively correlated with BL COMP (r=-0.62; p<0.01, CI:-0.32,-0.84), and BL→Y2 CILP change was negatively correlated with BL CILP (r=-0.73; p<0.01, CI:-0.53,-0.87). Neither BL COMP and CILP, nor BL→Y2 COMP and CILP changes were significantly correlated with each other (p=0.06 and p=0.13, respectively). BL COMP and BL CILP levels were not significantly associated with subregional cartilage thinning, thickening, or the non-directional change score (p≥0.19). BL→Y2 change in COMP was not significantly associated with BL→Y2 change in imaging markers. However, the association between BL→Y2 change in CILP and that in non-directional change score was significant (r=0.48; p<0.05).

Very similar observations were made in adolescent athletes (e.g.: r = -0.52; p=0.08 for BL→Y2 CILP change vs.

non-directional subregional cartilage thickness change), but these associations did not reach statistical significance, given the much smaller sample size.

Conclusions: This study compares subregional MRI-based cartilage thickness change, with baseline values and longitudinal change in two serum biomarkers (COMP and CILP). The above cartilage change scores are particularly useful in correlation analyses with serum biomarkers, because they describe structural tissue change in each direction (thinning and thickening) at a subregional level. A limitation of this study is the small sample size, in particular in the group of the adolescent athletes. Further, the study was exploratory and did not correct for multiple statistical testing. Nevertheless, our results indicate that longitudinal change in CILP and COMP are negatively correlated to BL values, and that change in CILP (but not change in COMP; nor BL CILP or COMP) is concurrently associated with subregional cartilage change.

Baseline (BL) values and longitudinal changes from BL to 2 year follow-up (Y2) in COMP and CILP

	Mature athletes		Adolescent athletes	
	Women	Men	Girls	Boys
BL COMP	12.6±3.9	13.1±4.3	11.6±4.5	16.5±5.1
Change COMP	0.2±2.57	0.67±4.87	-0.85±6.17	0.03±3.75
BL CILP	1.72±1.11	1.16±1.05	0.59±0.48	0.62±0.57
Change CILP	0.70±1.79	1.64±1.97	2.41±1.25	0.70±0.95
ThCTnS (mm)	-0.40±0.17	-0.52±0.42	-0.10±0.10	-0.22±0.20
ThCTkS (mm)	0.15±0.17	0.12±0.10	0.47±0.21	0.67±0.74
ThCChS (mm)	0.55±0.11	0.65±0.37	0.57±0.21	0.89±0.61

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