P106 – Table 1. Pearson correlation coefficients

	CTX-1I (N=55)	NTX-I (N=60)	HA (N=93)	COMP (N=91)	Epitope 846 (N=89)	CII Propeptide (N=93)
TQOL variable						
K-L 0-IV	0.298*	0.265*	0.302**	0.226*	-0.072	0.066
JSN 0-3	0.229	0.229	0.430***	0.297**	-0.131	0.032
Osteophyte 0-3	0.327*	0.243	0.277**	0.246*	0.002	0.069
Sclerosis 0-1	0.274*	-0.019	0.226*	0.195	-0.083	-0.034

*$p < 0.05$ (2-tailed test). **$p < 0.01$ level (2-tailed test). *$p < 0.001$ level (2-tailed test).

(BSP), Cartilage Oligomeric Matrix Protein (COMP), Bone Alkaline Phosphatase, Epitope 846, Hyaluronan, C-Reactive Protein (CRP), PIIANP, CII Propeptide, PINP, and urinary CTX-II and NTX-I. Bivariate Pearson correlation coefficients were calculated for each biomarker with each OA score.

Results: Significant correlations were observed with CTX-II, NTX-I, HA, and COMP, markers of collagen degradation, inflammation, and matrix turnover (Table 1). Correlations with the remainder of the biomarkers were not significant. TQOL severity averaged 35 (SD 19) for K-L grade and 7 (SD 7) for JSN. Findings contrasted with the positive correlation of biomarkers of synthetic activity observed in our prior report where individuals with hereditary OA, mean age 34 yrs, had K-L and JSN severity averaging 41 (SD 34) and 14 (SD 19) respectively.

Conclusions: The presence of OA in an older cohort demonstrated an increase in degradative/inflammatory markers, contrasting with increased PG and collagen synthesis in a younger hereditary OA population with greater disease severity. Although differences in pathophysiologic mechanisms between the groups cannot be excluded, findings suggest that biomarkers reflect disease duration as well as severity, and that biomarker responses precede changes in overt structural damage; snap-shot biomarker levels may only partially reflect disease evolution.

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INCREASED EXPRESSION OF CELL DEATH-ASSOCIATED C-JUN KINASE IN OSTEOARTHRITIC CARTILAGE

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Purpose: The aim of this study was to compare the expression of active cell-death associated c-jun protein and major pro-inflammatory cytokines IL-1 and TNF-α in synovial membrane and cartilage explants with that in control tissues.

Methods: Synovial membrane and cartilage explants from patients with OA and healthy controls were used for this experiment. Levels of cytokines IL-1α and TNFα in tissue extracts were measured by Immulite system and ELISA, respectively. Markers of apoptosis active caspase-3 and c-jun kinase were analyzed in paraffin embedded cartilage and synovial membrane samples by immunohistochemistry.

Results: The expression of phospho-c-jun was observed only in OA cartilage, but not in other examined tissues. Caspase-3 activity was higher in OA than in control cartilage (10% vs. $<$5% of positive cells), although there was no difference between OA and healthy synovial membranes. Furthermore, significantly higher expression of TNF-α was demonstrated in both OA synovial membrane and cartilage compared with counterpart control tissues. On the other side, IL-1α expression was significantly higher only in OA cartilage.

Conclusions: These data stress the role of pro-inflammatory cytokines and apoptosis of chondrocytes in the pathogenesis of osteoarthritis.

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TQOL-LITE: A SIMPLIFIED ASSESSMENT TOOL FOR TOTAL QUANTITATIVE OSTEOARTHRITIS (OA) LOAD

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Purpose: Current consensus suggests that biomarker correlations be based on total body burden of OA. In prior studies, we demonstrated positive correlations with proteoglycan and collagen synthetic activity in subjects with familial precocious hereditary OA utilizing a new assessment tool, Total Quantitative Osteoarthritis Load (TQOL). TQOL methodology defined OA cartilage involvement computed by joint disease severity multiplied by standardized MRI-derived joint cartilage volume at risk. Subsequent studies in a population of older subjects with idiopathic OA revealed significant correlations between TQOL scores and biomarkers CTX-II, NTX-I, HA, and COMP, markers of collagen degradation/inflammation and matrix turnover. To further validate a simplified TQOL instrument (TQOL-LITE), scores were calculated for this new instrument based on similar cartilage volumes for knee weight-bearing area (7 ml) and hip (9 ml), and compared to the previously obtained correlations utilizing the comprehensive classic TQOL measure.

Methods: Biomarker correlations were computed from data of 98 subjects, mean age 65 yrs (range 59-71), median duration 14 yrs, in all of whom x-rays of knees and hips were available. Kellgren-Lawrence (K-L) grade (0-IV) and Joint Space Narrowing (JSN) (0-3), were determined by an experienced musculoskeletal radiologist. Using standardized MRI-derived joint cartilage volumes, Total Quantitative Osteoarthritis Load (TQOL) scores were computed related to knee and hip OA. Biomarkers included serum Bone Sialoprotein (BSP), Cartilage Oligomeric Matrix Protein (COMP), Bone Alkaline Phosphatase, Epitope 846, Hyaluronan, C-Reactive Protein (CRP), PIIANP, CII Propeptide, PINP, and urinary CTX-II and NTX-I. Bivariate Pearson correlation coefficients were calculated for each biomarker with each classic TQOL OA score. Similar correlation coefficients were derived for TQOL-Lite using the Sum of Severity K-L scores and the Sum of Severity JSN scores.

Results: Significant correlations were observed for NTX-I, CTX-II, HA, and COMP, when using the Sum Severity scores (Table 1); correlations were most consistent with KL grade. No consistent significant correlations were seen with other biomarkers. Correlations were similar to results utilizing the classic TQOL assessment tool.

Conclusions: A simplified TQOL assessment tool based on