

**Cartilage collagen neopeptide C2C and clinical parameters in middle-aged patients with knee problems. Correlations of urinary output of C2C with cartilage lesions, KOOS values and functional abilities of lower limb.**

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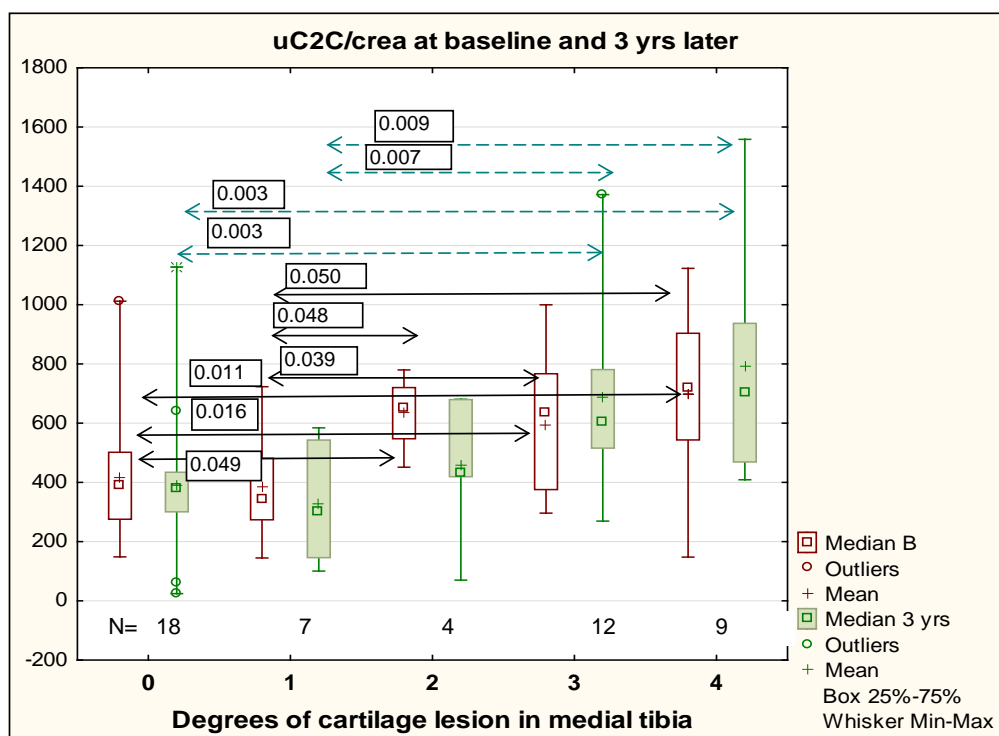
The aims of the study were to test: (i) the biomarker’s ability to differentiate between patients with and without knee cartilage lesion, (ii) if there is any correlation between urinary C2C output and clinical status of patients with early knee osteoarthritis, (iii) preferable way to express results, (iv) how the correlations might change with time (years).

**Material and methods.** We investigated 180 knee OA patients (68 male, 112 female) aged 36-62 (mean 50) yrs. For 112 patients the progression of the knee OA during the past 3 years was available. Standardised radiographs of the tibiofemoral(TF) and patellofemoral(PF) joints were assessed. Radiographic progression was defined as: (i)presence of osteophytes and/or joint space narrowing (JSN) in subjects with no previous radiographic OA or (ii)increase in their grade.

In a subset of 51 patients (25 male, 26 female, aged 32-56 yrs) the degree of cartilage lesion was assessed by an orthopedic surgeon on the Outerbridge (0-IV) and VAS (0-10) scales in the medial femoral, medial tibial and patellofemoral compartments. The clinical status of OA patients was established by KOOS questionnaire (self-assessment) and by four performance tests (up & go, raising from low chair, stairs-stepping, 30 m walk). The immunoassay used was C2C-HUSA™ (IBEX, Canada) that measures the C2C neopeptide fragments present in human urine samples. For statistical data analyses, T-test and Spearman’s rank correlation were used.

**Results:** The uC2C values were significantly higher for patients with tibial or femoral lesion degree 2 or higher both at baseline and 3 yrs after surgery (Fig. 1, B and 3 yrs).

**Fig. 1. Output of uC2C juxtaposed to different degrees of lesion in medial tibial cartilage**



Higher output of uC2C correlates with decline of the functional abilities of lower limb. The correlations were stronger when uC2C was expressed in ng/mmol creatinine (Table 2).

**Table 1. Correlations between urinary C2C and results of lower limb performance tests**

Performance tests	uC2C expressed in pg/ml urine			in ng/mmol creatinine	
	Valid (N)	Spearman (R)	p-value	Spearman (R)	p-value
UP&GO, sec	107	0.304	0.001	0.415	0.000009
Up from low chair, cm	106	0.372	0.00008	0.525	0.00000008
Step up left leg, cm	107	-0.354	0.0001	-0.448	0.000001
Step up right leg, cm	107	-0.360	0.0001	-0.484	0.0000001
30 m walk, sec	107	0.238	0.014	0.405	0.00001

**Conclusions: 1. Significantly higher excretion of uC2C is associated with grade 2+ cartilage lesion in knee joint.**

**2. Highly significant correlation appears between increased uC2C output and decline in the clinical functional parameters of the lower limb.**

**3. The above correlations are stronger when uC2C is expressed in ng/mmol creatinine.**

**Longitudinal study:Correlations between cartilage lesions of different localization and uC2C**

**Arthroscopy cases.** Urinary output of C2C was juxtaposed to the degree of cartilage lesion of the knee compartments (tibial medial, femoral medial, femoral lateral, patellofemoral) in 51 patients who had passed arthroscopic surgery. Significant correlations were observed between lesions and C2C levels both at baseline and after 3 years. At the same time, other factors e.g. patient age, also play an important and increasing role in analysis (Table 3).

**Table 2. Correlations between cartilage lesions and uC2C at baseline and 3 years later.**

	N	Spearman (rho)	p-value
<b>TABLE 2 A: BASELINE CORRELATIONS</b>			
uC2C/crea b & tib med degree	51	0.399	0.004
uC2C/crea b & fem med degree	51	0.285	0.043
uC2C/crea b & fem lat degree	51	0.278	0.048

**TABLE 2B: CORRELATIONS 3 YEARS LATER**

uC2C/crea 3yrs & tib med degree	51	0.529	0.0001
uC2C/crea 3yrs & fem med degree	51	0.439	0.001
uC2C/crea 3yrs & fem lat degree	51	0.365	0.008
uC2C/crea 3yrs & PF pat degree	51	0.273	0.053

**Table 3. Correlation between uC2C and age of the patient**

uC2C/crea b & age basel	51	<b>0.470</b>	0.0004
uC2C/crea 3yrs & age after 3yrs	51	<b>0.601</b>	0.000002

Summary. **We demonstrated that the output of uC2C correlates positively with degree of lesion of the knee cartilage as well as with patient age. The stronger correlation between biomarker C2C and cartilage status 3 years later seem to refer on progression of disease expressed by type II collagen degradation.**

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