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ORIGINAL ARTICLE

Osteocartilaginous metabolic markers change over a 3-week stage race in pro-cyclists

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Abstract

Evidence suggests that endurance and even recreational cycling may stimulate bone resorption; however, little is known about cartilage response to endurance cycling exercise. We investigated effort-dependent changes in bone turnover and cartilage biomarkers in blood and urine samples from elite cyclists during a 3-week stage race. Whole blood and urine samples were collected the day before the start of the race, at mid and end-race for serum and urinary CTx-I, NTx-I, PINP, COMP (only in serum), and CTx-II analysis by enzyme-linked immunosorbent assay. The values were corrected for plasma volume or creatinine excretion, respectively, and correlated with power output (corrected for body weight) and net energy expenditure. Bone marker concentrations in both serum and urine were slightly but significantly decreased. Among the cartilage degradation markers, only CTx-II was decreased, while COMP remained unchanged. The changes in bone and cartilage turnover indexes were correlated with the indexes of physical effort and energy consumption.

Strenuous physical effort, in the absence of mechanical loading, slows bone metabolism and only minimally affects cartilage turnover. Since changes in plasma and urine volume, which normally occur in exercising athletes, can mask these effects, biomarker concentrations need to be corrected for shifts in plasma volume and urinary creatinine for correct interpretation of the data.

Key Words: *Physical endurance, bone remodeling, cartilage, mechanical stress, energy expenditure*

Introduction

Road race cycling is one of the most physically demanding sports [1]. Recent research on physiological response during such endurance events as the Tour de France and the Giro d'Italia [2,3] has focused on the effects of strenuous exercise on bone metabolism [4–6]. In this model of non-weight-bearing sports, physical activity is performed without mechanical loading on the skeleton (i.e. ground reaction force [GRF]) [7] and only muscle contraction is applied to bone [6]. Mechanical loading is the most important determinant of bone mineral density (BMD), second to only genetic inheritance [8,9], while muscle contraction is unable to sustain anabolism in the absence of a certain degree of loading [6].

This notion is supported by the observation that BMD is lower in professional, amateur, and recreational cyclists, even among young riders, as compared with the general population [10]. From a metabolic point of view, exercise without loading stimulates osteoclast activity [4] and the osteocyte-related mechanosensitive response responsible for the increased production of sclerostin, but it does not affect osteoblast activity [6,11,12].

Although the beneficial effects of exercise, even when practiced recreationally, are widely recognized, little is known about the effect of strenuous exercise on articular cartilage metabolism [13]. Synthesis, assembly, and degradation of the cartilage extracellular matrix (in terms of turnover rate and quality) are known to be influenced by the forces applied to

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the matrix [14]. This means that both acute and chronic loading, as well as chronic unloading (i.e. immobility), can induce modifications in cartilage cell metabolism and improve articular response to external stimulation [13]. Cartilage oligomeric matrix protein (COMP), a non-collagenous glycoprotein that stabilizes the collagen fiber network by binding collagen II fibrils [15], is a useful biomarker for monitoring cartilage erosion in degenerative joint diseases [16–18]. Previous studies have highlighted its potential application as a biochemical marker to monitor the effects of acute and chronic exercise on cartilage metabolism. Serum COMP concentrations were found to be sensitive to running [19] and walking [20], and well-trained runners were noted to have higher basal serum COMP levels than untrained healthy counterparts [21]. In addition, cross-linked C-terminal peptide of collagen type II (CTx-II), a cartilage resorption marker detectable in serum, urine, and synovial fluid [22], is modified by mechanical loading, leading to changes in chondrocyte metabolism and possibly its degradation [13, 22].

To our knowledge, no studies to date have analyzed blood biochemical markers of cartilage turnover in cyclists or evaluated the relationship between these markers and those derived from bone metabolism. Therefore, we investigated the changes in blood and urinary bone turnover markers and cartilage degradation markers in blood and urine samples collected from elite cyclists during the 2012 Giro d'Italia 3-week stage race.

Method

In this observational, longitudinal prospective study, changes in blood and urinary biomarker values reflecting the physiological response to an intervention were analyzed.

Participants

A professional cycling team (Liquigas, formerly Liquigas-Cannondale), participating in the 95th Giro d'Italia, was followed during the race. The 2012 Giro d'Italia took place between 5 and 27 May, covering a total of 3502 km over 21 stages. The main features of the race are reported in Table I.

The team was composed of 9 male athletes; the mean age was 28.8 ± 3.6 years. Anthropometric parameters (weight and height) were measured in the morning, on fasting, before each stage; body-mass index (BMI) was calculated as weight/(height)^2. A summary of the anthropometric data is reported in Table II.

As in previous editions, the race organizers complied with the 'no-needle' policy, according to which therapies and drugs are allowed only for documented medical needs. The study was approved by the team's medical board and the reference institutional review board (ASL Milano 1); consent was obtained from all participants after having received a full explanation of the purpose and nature of the study.

Table I. Features of the 2012 Giro d'Italia stage race.

Day	Stage	Length (km)	Difference in elevation (m)	Stage type
−1*	R	/	/	/
1	1	8.7	50	TT
2	2	206	261	F
3	3	190	842	F
4	R	/	/	/
5	4	33.2	230	TT
6	5	209	466	F
7	6	210	4497	MM
8	7	205	4759	MM
9	8	229	5458	MM
10	9	166	1182	F
11	10	186	2261	MM
12*	11	255	2172	F
13	12	155	4249	MM
14	13	121	1800	F
15	14	206	4273	HM
16	15	169	5187	HM
17	R	/	/	/
18	16	173	1450	MM
19	17	186	8595	HM
20	18	149	1391	F
21	19	198	8441	HM
22	20	219	9491	HM
23*	21	30	58	TT

The table presents the data relative to the day of the stage (R: rest day), the length (in kilometers), the difference in elevation (in meters), and the type of each stage (TT: time trial, F: flat, MM: medium mountain, HM: high mountain). The asterisks (*) indicate the days of both blood and urine sampling.

Methodology

Diet regimen. The diet regimen was established by the team physicians who were also responsible for ensuring athletes' compliance. None of the participants took supplementation outside the nutritional regimen. Diet composition and caloric intake remained unchanged during the race. The total daily intake was about 6000 kcal derived from carbohydrates (45%), proteins (36%), and lipids (19%). Daily calcium and phosphorous intake was kept constant throughout the race (about 1700 mg/day and 3800 mg/day, respectively), as was creatinine consumption.

Power output and energy expenditure measurements. Power output (PO) and net energy expenditure (NEE) in the 2012 Giro d'Italia were reported in [6]. PO was mathematically derived from a power sensor (PowerMeter™, SRM GmbH, Jülich, Germany; imprecision ± 2%) integrated within the bike pedal. PO was normalized to body mass (PO/m). Energy expenditure (kcal) was automatically derived from the instantaneous PO; NEE was obtained by sub-

Table II. Changes in anthropometric measurements and indexes of effort.

	Day − 1	Day 12	Day 23	*p* value
Weight (kg)	67.9 (63.5–77.8)	66.4 (62.4–76.3)	67.3 (61.8–76.3)	n.s.
BMI (kg/m^2)	21.4 (19.8–22.7)	21.1 (19.5–22.0)	21.5 (19.3–22.1)	n.s.
Accumulated PO/m (W/kg)	0	36.54 (34.07–37.86)***	26.45 (24.87–28.03)****###	< 0.001
Mean PO/m (W/kg)	0	3.04 (2.84–3.15)***	3.31 (3.11–3.50)****###	< 0.001
Accumulated NEE (kcal)	0	41953 (39533–50996)***	31915 (29459–37892)****###	< 0.001
Mean NEE (kcal)	0	3496 (3294–4250)***	3989 (3682–4737)****###	< 0.001

The table shows the data of the between-sampling weight, BMI, mean and accumulated power output normalized to body mass (PO/m), and net energy expenditure (NEE) before (day − 1), at mid race (day 12), and at the end of the race (day 23). Data are expressed as median (5th–95th percentile). The right column reports the *p*-value of the Kruskal-Wallis test. Asterisks and hashtags refer to the paired comparisons for days 12 and 23 vs. day − 1 and day 23 vs. day 12, respectively (***/###$p < 0.001$).

tracting the basal consumption (indirectly measured with a QUARK RMR calorimeter (Cosmed S.r.l., Rome, Italy) from the total consumption. Accumulated and mean PO/m and NEE between samplings were calculated. Specifically, the mean and accumulated indices refer to either the mean or the sum, respectively, of consecutive measurements relative to the period preceding the sampling.

Blood and urine collection. The pre-analytical phase was strictly managed [23] and the Unione Cycliste Internationale (UCI) and World Anti-Doping Agency (WADA) guidelines for specimen collection and transport were followed. Blood and mid-stream urine were collected at about 08:00 the day before the start of the race day − 1 (T0), and at days 12 (T1) and 23 (T2) by standard venipuncture in sitting subjects after overnight fasting within 30 min after awakening. Sterile urine containers were used for urine collection. Serum (BD SSTII™ Advance, BD Vacutainer® Systems, Becton–Dickinson, Franklin Lakes, NJ, USA) and plasma (BD K2 EDTA 3.5 mL tubes) tubes were used, respectively, for biochemical and hematological analysis. The tubes were immediately inverted ten times and then allowed to clot for 30 min at room temperature according to the manufacturer's instructions. Blood and urine samples were stored at 4°C in a sealed box and delivered to the laboratory for immediate analysis (hematology) or aliquoted and stored at − 80°C until assayed (biomarkers). The delays between sampling and analysis/storage (T0: 12 h 30 min, T1: 3 h, T2: 1 h 30 min) were kept within the time limits established by WADA [24]. In the laboratory, sera were separated by centrifugation (1300 *g*, 10 min, 4°C) and immediately analyzed; K2 EDTA-anticoagulated blood was homogenized for 15 min prior to being analyzed, as recommended by WADA.

Biomarker measurement and hematological analysis. Bone turnover biomarkers in serum and urine were measured by monoclonal antibody-based enzyme-linked immunosorbent assays (ELISA) (USCN Life Science Inc., Wuhan, Hubei, China): C-terminal cross-linked telopetide of collagen type I (CTx-I) and N-terminal cross-linked telopetide of collagen type I (NTx-I) as bone resorption markers, and procollagen type I N-terminal propeptide (PINP) as a bone formation marker. The assay-specific sensitivities were 43.00 ng/L for CTx-I, 0.97 mg/L for NTx-I, and 12.20 ng/L for PINP. The intra- and inter-assay coefficient of variations (CV_w, CV_b) were < 10% and < 12%, respectively. Cartilage markers were measured in either serum (cartilage oligomeric protein [COMP]; BioVendor Inc., Brno, Czech Republic) or in both serum and urine (C-terminal cross-linked telopetide of collagen type II [CTx-II]; USCN Life Science Inc.) by monoclonal antibody-based ELISA. The sensitivities of CV_w, and CV_b (based on the actual concentrations) were 0.40 mg/L, < 4.0% and < 3.1%, respectively, for COMP, and 46.90 ng/L, < 10.0% and < 12.0%, respectively, for CTx-II. Serum and urine aliquots were centrifuged (1000 *g*, 20 min) before being assayed to eliminate particulate material. The absolute concentration of the analytes in the samples was calculated by interpolating the absorbance readings (VICTOR™ X^3 Perkin Elmer, Waltham, MA, USA) on their respective standard curves. All samples were evaluated in duplicate.

Urine creatinine was measured after centrifugation (1700 *g* for 10 min) using an enzymatic method on a Vitros autoanalyzer (Ortho-Clinical Diagnostics, Rochester, NY, USA). Urinary biomarker concentrations were normalized to [uCr].

Hemoglobin concentration ([Hb]) and hematocrit (Ht, %), used to calculate subject-specific plasma volume changes during the race, were determined on a Sysmex XE 2100 (Sysmex Corp., Kobe, Japan); the imprecision, as reported by the manufacturer, was < 2%. The analyzers were regularly calibrated and controlled according to internal and external quality control schemes during the study. Since exercise is known to affect plasma volume, repeated measurements of blood parameters were normalized to plasma volume changes (ΔPV) and calculated as described in Dill and Costill [25]. These data have been published in a previous study by our group [6].

Statistical analysis

Statistical analysis was performed using GraphPad Prism v5.0 software (GraphPad Software Inc., LaJolla, CA, USA). All values in the descriptive analysis are expressed as the median (5–95th percentile). Due to the small sample size, the data were considered non-normally distributed [26]. Friedman's test, with Dunn's correction, was used to compare the data over time. Correlation analysis was performed using Spearman's test, which was also used to evaluate the correlation between the trends of these parameters across the three time points. The significance level was set at 0.05.

Results

Anthropometric changes and metabolic effort

Table II shows the measurements in body weight, BMI, and physical effort indices. Body weight and BMI remained unchanged during the race. The indexes of physical effort changed significantly ($p < 0.001$): the accumulated PO/m and NEE were higher in the first half than in the second half of the race, indicating greater effort expended in the former.

Bone and cartilage biomarkers

The raw serum and urine biomarker values remained unchanged, but when the serum values were normalized to ΔPV%, all the markers, except for COMP, showed significant changes. The median concentrations of CTx-I, NTx-I, PINP, and CTx-II at T1 and T2 were lower as compared to T0. Additionally, PINP was significantly decreased between T1 and T2. The trends in serum marker concentrations are shown in Figure 1; detailed time-by-time raw and corrected values for each analyte are reported in Supplementary Table I, available online at http://informahealthcare.com/doi/abs/10.3109/00365513.2015.1057762.

The median uCr increased constantly and significantly (Figure 2 and Supplementary Table I, available online at http://informahealthcare.com/doi/abs/10.3109/00365513.2015.1057762). While in their raw form the urinary biomarker concentrations remained unchanged over the race, after correction for uCr they were all significantly decreased. Only uNTx-I was unchanged between T0 and T1 but it was decreased in the following comparisons. The trends in urinary biomarker concentrations are reported in Figure 3; detailed values are reported in Supplementary Table I, available online at http://informahealthcare.com/doi/abs/10.3109/00365513.2015.1057762.

Correlations

Correlation analysis confirmed a high level of concordance between the trends of all serum and urinary biomarkers, except for COMP. The indexes of effort did not correlate with COMP, while good to strong inverse correlations were found with the corrected concentrations of the other serum and urinary biomarkers. The correlations with the accumulated and mean NEE were in the same order of magnitude. The results of the correlation analysis are reported in Table III.

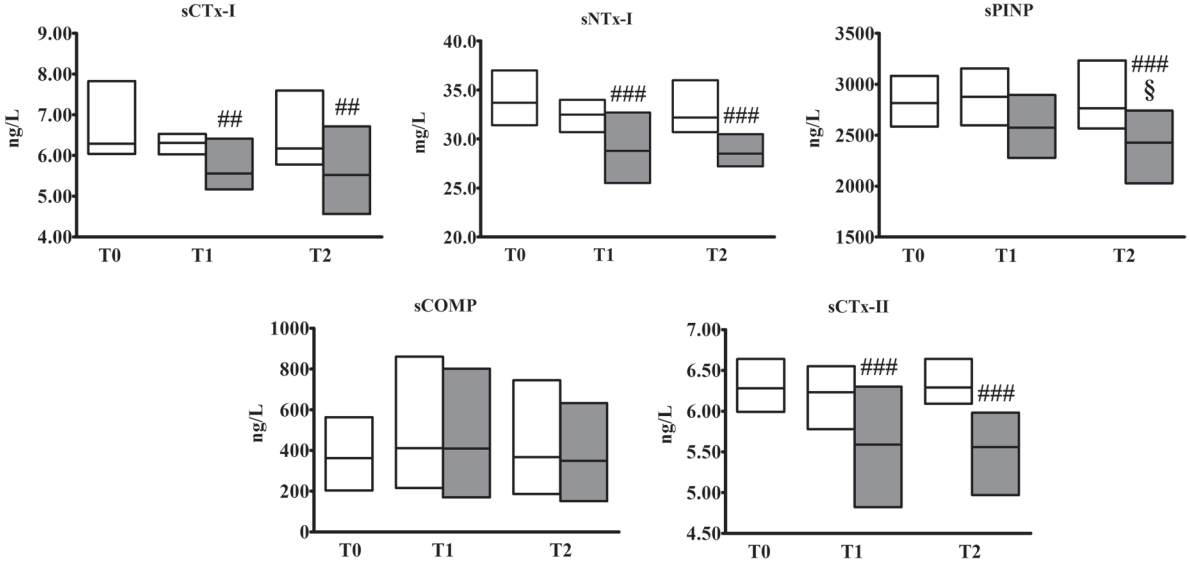

Figure 1. Changes in serum bone and cartilage biomarker concentrations over the race. The figure shows the trends of the raw (white bars) and ΔPV%-corrected (grey bars) serum concentrations of bone (CTx-I, NTx-I, PINP) and cartilage (COMP, CTx-II) turnover markers. The box plot shows the distribution width of the values (5th–95th percentile), for each time point and the median (internal line). # denotes a significant difference from T0 (## $p < 0.01$; ### $p < 0.001$).

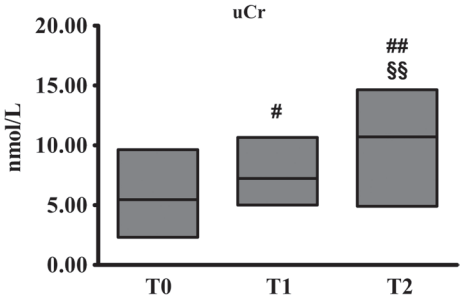

Figure 2. Changes in urinary excretion of creatinine over the race. The figure shows the trend of urinary creatinine concentrations. The box plot shows the distribution width of the values (5th–95th percentile) for each time point, and the median (internal line). # denotes a significant difference from T0; § denotes a significant difference from T1 (#/§ $p<0.05$; ##/§§ $p<0.01$; ###/§§§ $p<0.001$).

Discussion

The aim of the present study was to investigate the changes in bone turnover and cartilage degradation markers in blood and urine in elite cyclists over a 3-week cycling stage race in order to determine whether a correlation with the indexes of physical effort exists.

During previous Giro d'Italia races involving a fully comparable population of athletes, an imbalance in bone turnover toward resorption was found [7,27]. Furthermore, recent studies have demonstrated that cycling training, professional or even recreational, through adolescence [10] and adulthood [28] negatively affects BMD, reducing peak bone mass at different anatomical sites. This has several implications for preventive medicine, foremost among which is the selection of exercise modalities according to age group and health condition. While cycling provides numerous recognized health benefits, including enhanced cardiovascular fitness and the associated reduction in mortality rates [29,30], it does not improve bone mass (in the more optimistic assumption) [29]. This point deserves consideration since cycling, as an aerobic activity, is often recommended to prevent, or even treat, osteopenia. Despite the emerging evidence for a negative effect of long-term cycling training on bone, whether the reduction in BMD is due to increased resorption or reduced deposition of new bone remains controversial. To our knowledge, there are no studies on cartilage response to such a long-term physical activity.

We have previously investigated different endocrine-related mechanisms involved in the regulation of bone turnover during multiday races. Over the race, osteoblast activity remains unchanged while bone resorption by osteoclasts is slightly greater, as demonstrated by the increased activity of serum TRAP5b. This imbalance is uncoupled from hormonal regulation by cortisol and testosterone [4]. Furthermore, although muscular traction is the main anabolic stimulus for bone remodeling, the lack of mechanical loading in cycling stage races induces sclerostin production, which inhibits pro-anabolic Wnt signaling in pre-osteoblasts [6]. The prolonged strenuous endurance effort in the absence of loading, independent of parathyroid hormone (PTH)- and 25-hydroxyvitamin D, thus causes bone resorption which increases blood phosphorous concentration and stimulates, in turn, the osteocytes to produce phosphatonin fibroblast growth factor (FGF) 23 [5].

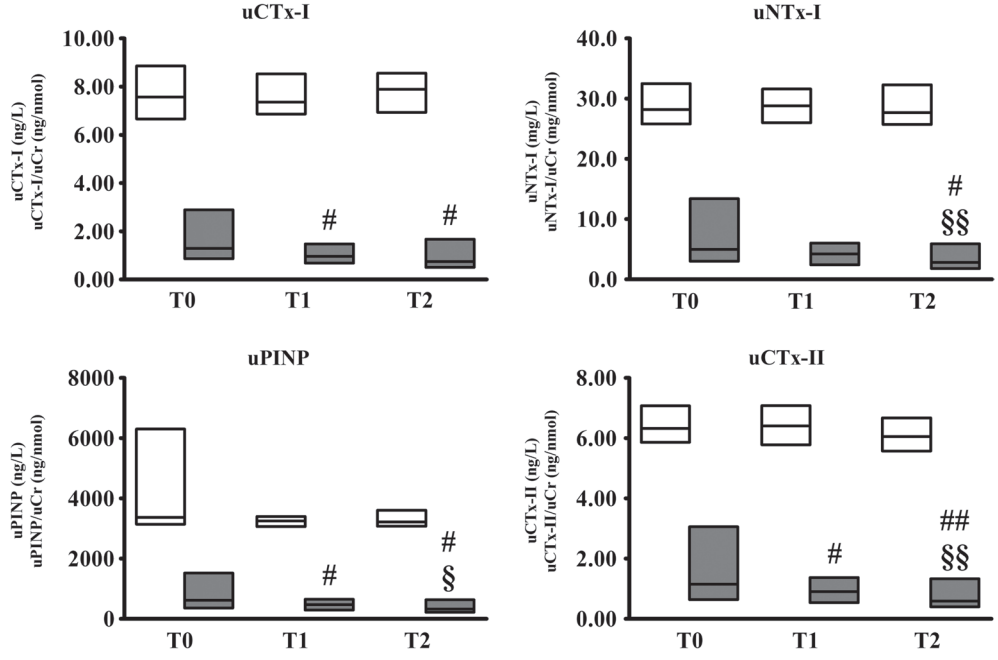

Figure 3. Changes in urinary concentrations of bone and cartilage biomarkers over the race. The figure shows the trends of the raw (white bars) and uCr-corrected (grey bars) urinary concentrations of the bone (CTx-I, NTx-I, PINP) and cartilage (CTx-II) turnover markers. The box plot shows the distribution width of the values (5th–95th percentile) and the median (internal line). # denotes a significant difference from T0; § denotes a significant difference from T1 (#/§ $p<0.05$; ##/§§ $p<0.01$; ###/§§§ $p<0.001$).

Table III. Correlations between bone and cartilage biomarker trends and indices of physical effort.

Serum			Urine		
	r	*p*-value		r	*p*-value
sCTx vs.			uCTx vs.		
sNTx-I	0.61	<0.001	uNTx−I	0.98	<0.001
sPINP	0.51	<0.001	uPINP	0.89	<0.001
sCTx-II	0.72	<0.001	uCTx−II	0.97	<0.001
sCOMP	*−0.19*	*0.346*			
sNTx-I vs.			uNTx−I vs.		
sPINP	0.67	<0.001	uPINP	0.91	<0.001
sCTx-II	0.85	<0.001	uCTx−II	0.99	<0.001
sCOMP	*0.10*	*0.603*			
sPINP vs.			uPINP vs.		
sCTx-II	0.71	<0.001	uCTx−II	0.89	<0.001
sCOMP	*−0.18*	*0.362*			
sCTx-II					
sCOMP	*−0.02*	*0.928*			
Accumulated PO/m vs.			Accumulated PO/m vs.		
sCTx vs.	−0.63	<0.001	uCTx vs.	−0.47	0.013
sNTx-I	−0.76	<0.001	uNTx−I	−0.44	0.021
sPINP	−0.52	<0.001	uPINP	−0.58	<0.001
sCTx-II	−0.73	<0.001	uCTx−II	−0.42	0.027
sCOMP					
Mean PO/m vs.			Mean PO/m vs.		
sCTx vs.	−0.68	<0.001	uCTx vs.	−0.51	0.007
sNTx-I	−0.78	<0.001	uNTx−I	−0.49	0.009
sPINP	−0.62	<0.001	uPINP	−0.63	<0.001
sCTx-II	−0.76	<0.001	uCTx−II	−0.48	0.011
sCOMP					
Accumulated NEE vs.			Accumulated NEE vs.		
sCTx vs.	−0.65	<0.001	uCTx vs.	−0.49	0.009
sNTx-I	−0.76	<0.001	uNTx−I	−0.47	0.014
sPINP	−0.59	0.001	uPINP	−0.60	0.001
sCTx-II	−0.75	<0.001	uCTx−II	−0.45	0.019
sCOMP	*0.07*	*0.715*			
Mean NEE vs.			Mean NEE vs.		
sCTx vs.	−0.69	<0.001	uCTx vs.	−0.53	0.004
sNTx-I	−0.77	<0.001	uNTx−I	−0.52	0.006
sPINP	−0.68	<0.001	uPINP	−0.64	<0.001
sCTx-II	−0.77	<0.001	uCTx−II	−0.50	0.008
sCOMP	*0.21*	*0.303*			

The table presents the correlations between serum/urinary marker concentrations (corrected for either plasma volume changes or urinary creatinine concentration) and between these markers and the indices of physical effort. Correlations not reaching statistical significance are given in italics.

Two systematic revisions of the literature highlighting the effects of cycling on BMD have reported comparable results; however, the studies differed widely in study population composition, data source, comparison group, and cycling level. In their review of 13 studies, Nagle and Brooks concluded that, despite the limited quality of the published studies, the cross-sectional data indicate that cyclists may be at risk for low bone mass, particularly at the lumbar spine [31]. Olmedillas et al. reviewed 31 studies and reported that BMD is lower in regularly training adult road cyclists than in other types of cyclists (i.e. mountain bikers) or in those who combined cycling with other sports [29].

The results of our study add a new piece of information to this complex picture. We found a slowdown in both the bone turnover rate and cartilage turnover, with a strong inverse correlation with the indices of physical effort. When the data were normalized to plasma volume changes and urinary creatinine excretion, all serum and urinary biomarkers except serum COMP were decreased. The reason for this decrease could be the slowdown in bone and cartilage metabolism. Comparing these results with previous data, particularly with the evidence for osteoclast activation [4], increased plasma sclerostin (SOST), and increased excretion of calcium and phosphorous over the race [6], it could be hypothesized that the slowdown in bone cell metabolism is counteracted by an increased dissolution of the mineral portion of the matrix. This hypothesis fits well with radiological findings of a specific reduction in BMD rather than in total bone mass [10].

We selected the biochemical markers for this study to complete the panel of the markers analyzed in previous studies in these athletes. We used the two

markers the International Osteoporosis Foundation (IOF) and the International Federation of Clinical Chemistry (IFCC) recommend to monitor bisphosphonate treatment in osteoporosis: procollagen type I N-propeptide (PINP) and C-terminal crosslinking telopeptide of type I collagen (CTx-I) [32]. Both markers are useful in monitoring the effects of antiresorptive therapies, though few data are available about their changes in different physiological conditions (i.e. physical activity) and, specifically, no studies to date have investigated their changes during physical activity in the absence of loading [23].

As concerns the cartilage turnover markers, it seems that 21 days of competitive cycling had no deleterious effects on cartilage metabolism. CTx-II, although poorly characterized in terms of tissue and processing origins, is known to rise with cartilage degradation (as seen in rheumatoid arthritis and osteoarthritis) [22], as recently confirmed by a large-scale meta-analysis on osteoarthritis patients [33]. COMP, a non-collagenous protein expressed mainly in the extracellular matrix of cartilage, ligament, and tendon, is a marker of joint destruction associated with osteoarthritis, rheumatoid arthritis, joint trauma, and intense activity [34]. Moreover, serum COMP concentrations are a function of both the intensity and the kind of mechanical load applied to the skeleton [35]. Previous reports have shown that both CTx-II [22] and COMP [13,36] are increased after running activities, indicating stress on the articular cartilage from ground reaction forces [37]. In cycling, where such forces are absent, the level of these markers in the cyclists was unaffected (COMP) or even decreased (CTx-II). This observation is corroborated by the data by O'Kane and colleagues who showed that in a non-weight-bearing activity like swimming the average serum CTx-II concentrations are lower than those of cross-country runners, downhill runners or rowers [22,38].

Overall, our data on COMP and CTx-II, together with those previously published [13,22] suggest that the unchanged/lower serum or urinary concentrations of cartilage degradation markers during cycling (as well as swimming) can be associated with minimal biomechanical stress on joints. Indeed, as long recognized, joint-stressing activities (i.e. distance running or rowing) increase the levels of these markers. Furthermore, the absence of any variation in serum COMP, even after correction for plasma volume, strongly argues in favor of the hypothesis that cycling, by minimally stressing the joints, has no deleterious effects on articular cartilage metabolism.

Importantly, the changes in biochemical marker levels became evident only after the values were corrected for plasma volume shift and creatinine excretion. Although this is generally applied to urinary markers [39], it is not always done for blood parameters. But because physical activity affects plasma volume by inducing either hemodilution or hemoconcentration and because riders are generally allowed to assume liquids at libitum during cycling races, repeated blood parameter measurements should be always corrected for plasma volume changes to understand whether the modifications are real or apparent [25]. Moreover, further strengthening our data on urinary concentrations is the fact that kidney function, and the estimated glomerular filtration rate (eGFR) in particular, are not affected during stage races [40].

The main limitation of this study is represented by the small sample size; however, the population is highly selected and trained to compete in strenuous endurance events. In fact, there are only 800 professional athletes worldwide according to the international cycling ranking.

Cycling is one of the few sports in which no other activity other than cycling is performed. This means that physical activity is generally 'limited' to pedaling without the possibility to compensate for the lack of mechanical loading. As such, cycling cannot be considered a complete sports discipline. The slower bone turnover in elite cyclists, as demonstrated by this study and previous studies, signals the need to monitor bone health in cyclists and other endurance athletes. In cases of identified low BMD, the team physician should prescribe complementary exercises to recover bone strength.

In conclusion, the main findings of the present study are consistent with previous data and show that the reduction in bone turnover rate indicates a slowdown of bone metabolism associated with depletion of the mineral component of the bone matrix but without any deleterious effects on articular cartilage.

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Supplementary material available online

Supplementary Table I, available online at http://informahealthcare.com/doi/abs/10.3109/00365513.2015.1057762.