Difference in Articular Degeneration Depending on the Type of Sport*

Diferença na degeneração articular de acordo com o tipo de esporte

Pedro Baches Jorge[1] Jan Willem Cerf Sprey[1] Guilherme Morgado Runco[1] Marcos Vaz de Lima[1] Nilson Roberto Severino[1] Claudio Santili[1]

[1] Sports Trauma Group, Departament of Orthopedics and Traumatology, Faculdade de Ciências Médicas, Irmandade de Misericórdia da Santa Casa de São Paulo, São Paulo, SP, Brazil

Address for correspondence Pedro Baches Jorge, MD, Clínica SO.U - Matriz, Rua Barata Ribeiro, 398, 3° andar, Bela Vista, São Paulo, 01308-000, SP, Brazil (e-mail: pbj1980@hotmail.com).

Rev Bras Ortop 2019;54:509–515.

Abstract

Objective To determine whether type-II collagen degradation is determined by the type of sport. Carboxy-terminal telepoptide of type-II collagen (CTX-II), a serum biomarker of collagen degradation, was measured in athletes who play different sports, and was compared with matched controls.

Methods The sample size consisted of 70 female participants aged between 18 and 25 years, 15 of whom were members of a soccer team, 10 of a *futsal* (a variant of association football played on a hard court) team, 10 of a handball team, 18 of a volleyball team, and 7 of a swimming team. A total of 9 age- and sex-matched individuals with sedentary lifestyles were included in the control group. 3-mL blood samples were collected from each participant, and they were analyzed using an enzyme-linked immunosorbent assay (ELISA).

Results A comparison of the CTX-II concentrations of the players of different sports with those of the control group resulted in the following *p*-values: volleyball ($p = 0.21$); soccer ($p = 0.91$); handball ($p = 0.13$); *futsal* ($p = 0.02$); and swimming ($p = 0.0015$). Therefore, in the investigated population, *futsal* represented the highest risk for type-II collagen degradation and, consequently, for articular cartilage degradation, whereas swimming was a protective factor for the articular cartilage. No statistically significant difference was found in the body mass index among the groups.

Conclusion *Futsal* players are exposed to greater articular degradation, while swimmers exhibited less cartilage degradation compared with the control group in the study population, suggesting that strengthening the periarticular muscles and aerobic exercise in low-load environments has a positive effect on the articular cartilage.

Keywords

- cartilage
- biomarkers
- arthrosis
- athletes

* *Published Originally by Elsevier Editora Ltda.*

received
October 31, 2017
accepted
February 21, 2018

DOI https://doi.org/10.1016/j.rboe.2018.02.012.
ISSN 0102-3616.

Resumo

Objetivo Determinar se a degradação de colágeno tipo II é determinada pelo tipo de esporte. O telopeptídeo carboxiterminal do colágeno tipo II (CTX-II), biomarcador de soro de degradação de colágeno, foi medido em atletas de esportes diferentes e comparado aos controles correspondentes.

Métodos A amostra consistiu em 70 participantes do sexo feminino com idade entre 18 a 25 anos, das quais 15 eram membros de uma equipe de futebol, 10 de uma equipe de futebol de salão, 10 de uma equipe de handball, 18 de uma equipe de vôlei, e 7 de uma equipe de natação. Foram incluídos no grupo de controle 9 indivíduos sedentários, pareados por idade e sexo. Uma amostra de sangue de 3 mL foi coletada de cada participante e analisada usando um ensaio imunossorvente ligado a enzima (ELISA, do inglês *enzyme-linked immunosorbent assay*).

Resultados Uma comparação das concentrações de CTX-II das praticantes de diferentes esportes em comparação com o grupo de controle apresentou os seguintes valores de p: voleibol ($p = 0{,}21$); futebol ($p = 0{,}91$); handebol ($p = 0{,}13$); futebol de salão ($p = 0{,}02$) e natação ($p = 0{,}0015$). Portanto, na população investigada, o futebol de salão apresentou o maior risco de degradação do colágeno tipo II, e, consequentemente, de degradação da cartilagem articular, enquanto que a prática de natação foi um fator protetor para a cartilagem articular. Não foi observada diferença estatisticamente significativa no índice de massa corporal entre os grupos.

Conclusão As jogadoras de futebol de salão estão expostas a uma maior degradação articular, enquanto que as nadadores apresentam menor degradação da cartilagem em comparação com o grupo de controle na população estudada, o que sugere que o fortalecimento dos músculos periarticulares e o exercício aeróbico em ambientes de baixa carga têm um efeito positivo na cartilagem articular.

Palavras-chave

- cartilagem
- biomarcadores
- artrose
- atletas

Introduction

The articular cartilage is a specialized avascular, aneural tissue that covers the bony parts of the diarthrodial joints. Its function is to facilitate smooth motion via its low frictional coefficient, in addition to absorbing shock and supporting load in several planes.[1,2]

The preservation of the articular cartilage depends on maintaining the integrity of its molecular structure.[1] The main macromolecules that comprise cartilage are collagen and proteoglycans; during the course of life, the activity of the chondral cells is determined by several autocrine and non-autocrine factors that result in the maintenance or destruction of articular homeostasis. Osteoarthrosis is a common condition in the elderly, but it can also affect young people who are subjected to excessive articular loads.[1–17]

In adults, the activation of the articular function within the physiological limits of load and work frequency is crucial to maintain joint health;[3–6,9,13] therefore, joints working below the required levels are also at risk of degenerating.[10]

Work frequency and articular overload are important factors in articular destruction, which is characterized by damage to cartilaginous tissue.[2] Indeed, excessive exposure to overload leads to early articular wear,[2–6,9,10,13] which is then perpetuated by an inflammatory cascade that affects all of the articular tissue.[16] Therefore, high-performance athletes subjected to excessive training loads over a short period of time are at a higher risk of developing articular damage; the knees, in particular, tend to be overexposed in most sports. As a function of the constant demand for maximal performance, early articular wear and functional disabilities might result in the end of an athletic career.

Most patients are diagnosed in the advanced stages of arthrosis, when a series of metabolic events has already occurred, and the process is likely past the point at which pharmacological and surgical interventions are truly effective.[18]

The products of collagen matrix degradation might serve as useful markers of the severity and progression of arthrosis. Such products might be measured in the synovial fluid, blood or urine, and thus supply important information for the early diagnosis of arthrosis.

Regarding Articular Collagen

Collagen represents 50 to 60% of the dry weight of the cartilage. Its fibers form a dense network that gives shape to this tissue. The most important mechanical properties of collagen are resistance and resilience, which are transmitted to the cartilage.[1]

Type-II collagen is specific to cartilage, and represents nearly 98% of the total collagen content in this tissue.[1]

Type-II collagen is the largest macromolecule that composes the cartilage, and it consists of three identical polypeptide chains arranged in a triple helix. Each such chain is synthesized as a pro-chain that contains large pro-peptides at its ends, which are separated from the central part by telopeptides. During the maturation of type-II collagen molecules, proteases

cleave the pro-peptides; thus, the mature structure consists of the central part of the triple helix and telopeptides.

When the articular components degrade, they are expelled from their source tissue and are measured most accurately in the articular fluid. However, when studying osteoarthritis, the measurement of biomarkers in the blood and urine is made using less aggressive methods that are still effective and precise.[1]

The carboxy-terminal telopeptide of type-II collagen (CTX-II) is a biomarker of articular degradation. The use of CTX-II as a biomarker, in addition to its direct relationship with the radiological grade of disease, clinical scores and severity of cartilaginous lesions, is well established in the literature.[2,18–28] Thus, the measurement of CTX-II appears to be an effective method to investigate the turnover of type-II collagen.

The present study aimed to detect the early degradation of articular type-II collagen by measuring CTX-II levels in the blood of athletes performing different sports and comparing them with those of a control group. We sought to establish whether sport participation is a risk factor for early articular degradation in our country, and which sport was the most harmful to articular type-II collagen in the investigated population.

Materials and Methods

The present study was performed at the Sports Trauma Group of the Department of Orthopedics and Traumatology of our institution. The study was approved by the institutional ethics committee (number 244/11), and signed informed consent was obtained from every participant.

The study population consisted only of females aged between 18 and 25 years, who were members of competitive sports teams, including soccer, *futsal* (a variant of association football played on a hard court), handball, volleyball and swimming, at Clube Atlético São José, which is a partner of the Sports Trauma Group of our institution. The participants had to have between 5 and 8 years of training in the sport, and none of the athletes participated in other sports.

Patients with articular pain undergoing treatment, history of articular orthopedic surgery or of untreated articular pain due to any cause were excluded from the study, and all individuals in this group were female.

A total of 9 individuals with sedentary lifestyles who met the inclusion criteria formed the control group. None of them had ever participated in sports in a competitive way.

A total of 70 female participants aged between 18 and 25 years were included: soccer ($n = 15$), *futsal* ($n = 10$), handball ($n = 10$), volleyball ($n = 18$) and swimming ($n = 7$); 9 individuals with sedentary lifestyles were included in the control group.

A total of 3 mL of blood was collected from each participant by simple venous puncture of the non-dominant upper limb using a vacuum collection kit, in which there is contact of the sample with ethylenediaminetetraacetic acid (EDTA), which does not affect the result, and the body mass index (BMI) was calculated as the weight divided by the height squared of each person.

The blood was centrifuged, and the plasma was stored at -80◦C until all of the blood samples were ready for analysis, in a total of 23 days, because the test was performed in the same day. The samples were analyzed to detect human CTX-II using enzyme-linked immunosorbent assays (ELISAs; Hu CTX-II kit, Cusabio Biotech, Houston, TX, US). This test has 100% of specificity for human CTX-II without any cross-reactions, and a minimum level of detection of 0.2 ng/mL, which is informed by the manufacturer.

The results were compared using the Student *t*-test with a 95% confidence interval (95%CI), and values of $p < 0.05$ were considered statistically significant.

Results

A total of 70 female participants aged between 18 and 25 years were included: soccer ($n = 15$), *futsal* ($n = 10$), handball ($n = 10$), volleyball ($n = 18$) and swimming ($n = 7$); 9 individuals with sedentary lifestyles were included in the control group.

The average age for the control group was of 22.6 years, the mean BMI was of 22.3, and the mean concentration of CTX-II was of 0.453 ng/mL (►**Table 1**).

Among the 18 volleyball players, the average age was of 18.3 years, the mean BMI was of 22.33, and the mean CTX-II was of 0.429 ng/mL; this team trained 36 hours per week (►**Table 2**).

Among the 15 soccer players, the average age was of 22.36 years, the mean BMI was of 22.06, and the mean CTX-II was of 0.456 ng/mL; this team trained 15 hours per week (►**Table 3**).

Among the *futsal* players, the average age was of 18.5 years, the mean BMI was of 22.21, and the mean CTX-II was of 0.542 ng/mL; this team trained 15 hours per week (►**Table 4**).

Among the handball players, the average age was of 18.9 years, the mean BMI was of 22.88, and the mean CTX-II was of 0.416 ng/mL; this team trained 25 hours per week (►**Table 5**).

Among the swimmers, the average age was of 18.9 years, the mean BMI was of 20.71, and the mean CTX-II was of 0.373; this team trained 12 hours per week (►**Table 6**).

Table 1 Control group

Participant	Age (years)	Height (meters)	Weight (kilos)	BMI	CTX-II (ng/ml)
1	22	1.7	48	16.6	0.486
2	21	1.7	65	22.49	0.427
3	22	1.5	63	28	0.443
4	24	1.64	50	18.59	0.461
5	22	1.71	64	21.88	0.474
6	23	1.57	53	21.5	0.45
7	25	1.7	72	24.91	0.442
8	22	1.68	53	18.77	0.432
9	22	1.59	67	26.5	0.459

Abbreviations: CTX-II, carboxy-terminal telepeptide of type-II collagen; BMI, body mass index.

Table 2 Volleyball

Athlete	Age (years)	Height (meters)	Weight (kilos)	BMI	CTX-II (ng/ml)
10	18	1.85	80	23.37	0.421
11	18	1.71	74	25.3	0.418
12	18	1.79	66.6	20.78	0.426
13	19	1.8	70	21.6	0.424
14	19	1.83	75	22.39	0.637
15	20	1.86	66	19.07	0.449
16	20	1.82	67.5	20.37	0.443
17	18	1.66	54	19.59	0.407
18	18	1.77	66	21.06	0.615
19	19	1.86	75	21.67	0.451
20	23	1.73	83	27.73	0.509
21	18	1.79	86	26.84	0.506
22	18	1.62	52	19.81	0.577
23	18	1.79	70	21.84	0.591
24	18	1.82	71	21.43	0.434
25	18	1.86	80	23.12	0.418
26	18	1.75	68	22.2	0.429
27	18	1.62	61	23.24	0.429

Abbreviations: CTX-II, carboxy-terminal telepeptide of type-II collagen; BMI, body mass index.

Table 3 Soccer

Athlete	Age (years)	Height (meters)	Weight (kilos)	BMI	CTX-II (ng/ml)
28	25	1.61	52	20.06	0.526
29	24	1.67	74	26.53	0.498
30	18	1.75	60	19.59	0.466
31	21	1.62	59	22.48	0.499
32	19	1.68	56	17.84	0.527
33	20	1.56	52	21.37	0.495
34	25	1.68	70	24.8	0.476
35	24	1.57	57	23.12	0.475
36	22	1.63	62	23.33	0.496
37	22	1.6	57	22.26	0.46
38	24	1.54	50	21.08	0.441
39	25	1.7	67	23.18	0.431
40	19	1.65	65	23.87	0.136
41	19	1.76	60	19.36	0.136
42	21	1.62	62	23.33	0.507

Abbreviations: CTX-II, carboxy-terminal telepeptide of type-II collagen; BMI, body mass index.

The following *p*-values were obtained by comparing the different sports to the control group using the Student *t*-test: volleyball, $p = 0.21$ (►**Fig. 1**); soccer, $p = 0.91$ (►**Fig. 2**); handball, $p = 0.13$ (►**Fig. 3**); *futsal*, $p = 0.02$ (►**Fig. 4**); and swimming, $p = 0.0015$ (►**Fig. 5**).

Table 4 *Futsal*

Athlete	Age (years)	Height (meters)	Weight (kilos)	BMI	CTX-II (ng/ml)
43	18	1.65	59	21.67	0.512
44	18	1.73	59	19.71	0.475
45	18	1.55	45	18.73	0.552
46	18	1.6	60	23.44	0.643
47	19	1.7	68	23.53	0.473
48	18	1.59	60	23.73	0.591
49	20	1.67	65	23.31	0.771
50	19	1.58	52	20.83	0.522
51	19	1.62	64	24.39	0.445
52	18	1.49	50	22.71	0.431

Abbreviations: CTX-II, carboxy-terminal telepeptide of type-II collagen; BMI, body mass index.

Table 5 Handball

Athlete	Age (years)	Height (meters)	Weight (kilos)	BMI	CTX-II (ng/ml)
53	19	1.61	56	21.6	0.419
54	18	1.71	71	24.28	0.439
55	18	1.75	69	22.53	0.451
56	18	1.67	48	17.21	0.41
57	21	1.69	83	29.06	0.522
58	19	1.68	69	24.44	0.297
59	18	1.6	55	21.48	0.471
60	19	1.82	72	21.73	0.332
61	21	1.7	65	22.49	0.358
62	18	1.71	70	23.93	0.458

Abbreviations: CTX-II, carboxy-terminal telepeptide of type-II collagen; BMI, body mass index.

Table 6 Swimming

Athlete	Age (years)	Height (meters)	Weight (kilos)	BMI	CTX-II (ng/ml)
63	18	1.73	63	21.04	0.345
64	18	1.64	54	20.07	0.365
65	19	1.63	55	20.70	0.45
66	19	1.68	57	20.19	0.323
67	18	1.71	61	20.86	0.356
68	19	1.69	60	21	0.371
69	21	1.74	64	21.13	0.402

Abbreviations: CTX-II, carboxy-terminal telepeptide of type-II collagen; BMI, body mass index.

Thus, *futsal* represented the highest risk for type-II collagen degradation and consequently for articular cartilage degradation, whereas swimming was a protective factor for the articular cartilage in the investigated population.

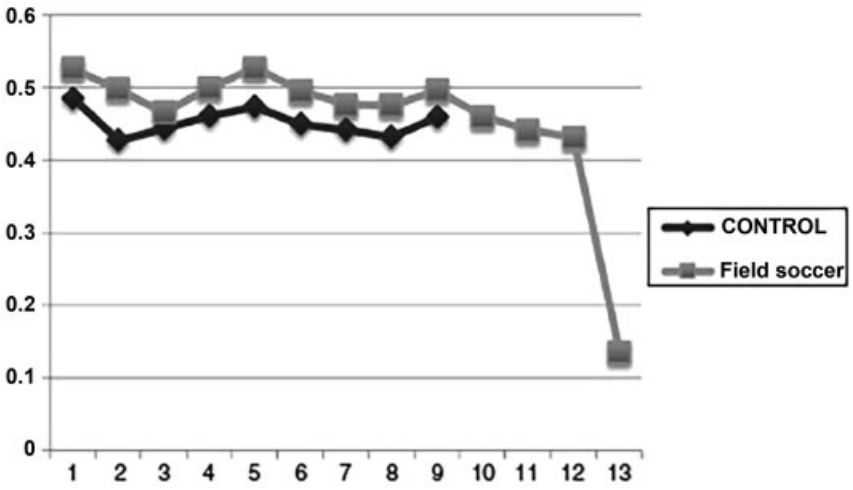

Fig. 1 Comparison between the CTX-II concentration results of the control group and of the soccer players.

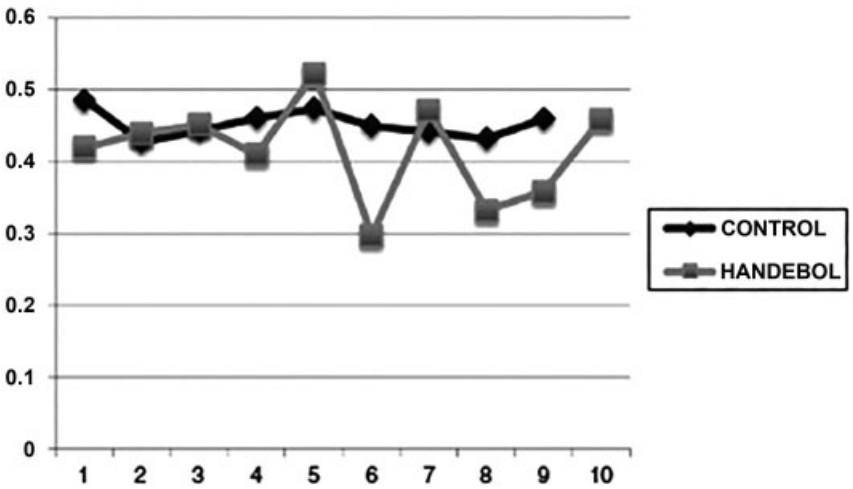

Fig. 2 Comparison between the CTX-II concentration results of the control group and of the handball players.

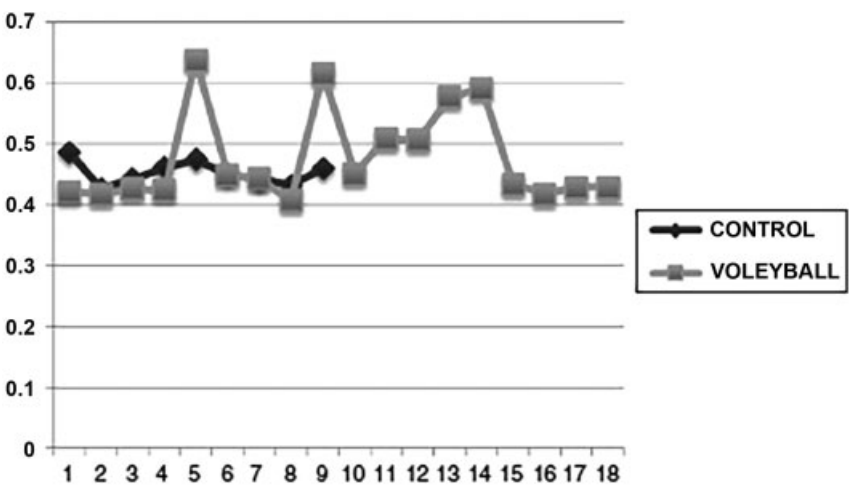

Fig. 3 Comparison between the CTX-II concentration results of the control group and of the volleyball players.

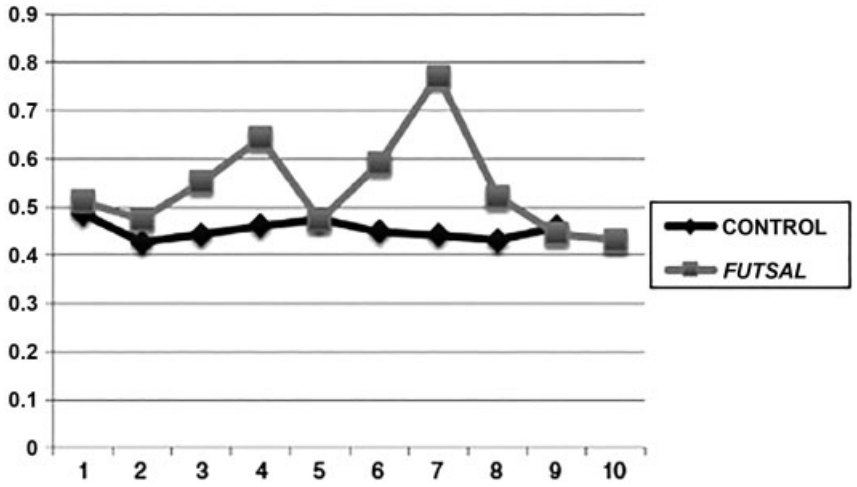

Fig. 4 Comparison between the CTX-II concentration results of the control group and of the *futsal* players.

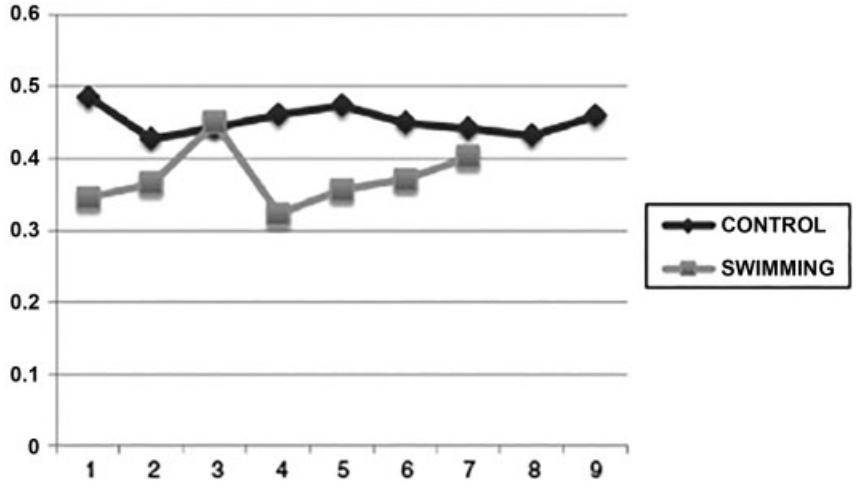

Fig. 5 Comparison between the CTX-II concentration results of the control group and of the swimmers.

Discussion

Currently, prevention is emphasized over treatment; thus, the early diagnosis of osteoarthrosis is of paramount importance. In the case of athletes, early diagnosis is even more important because their occupation depends directly on the health of their joints.

Because the first cleavage of articular type-II collagen catalyzed by collagenases releases the CTX-II epitope, which can be measured in the blood, urine and synovial fluid, it is a powerful tool for the early diagnosis of articular wear.

Type-II collagen is present in every synovial joint; however, the concentration of CTX-II is higher in patients with knee and hip arthrosis compared with the overall population.[27] CTX-II is a biomarker for cartilage destruction, and an increased level is a positive predictor for articular space reduction.[27,28]

When we measured the concentration of CTX-II in athletes who play different sports, we sought to detect whether the risk of overload and early articular destruction would be higher for any particular sport. Although the sample size for each sport might appear small, these are closed teams subjected to the same training load and, in theory, to the same articular overload.

In our study population, the volleyball, handball and soccer players did not exhibit higher type-II collagen degradation, although they participated intensively in high-impact activities. Perhaps this finding is explained by the fact that the study population was very young, and, for these three modalities, either the terrain or the shoes are able to absorb the shock.

Type-II collagen degradation was highest among the *futsal* players, and was significantly different than that of the control group (►**Fig. 4**) using a 95%CI. This discrepancy was likely because this sport is played on a rigid floor, requires shoes that do not absorb shock, and has frequent shifts in direction overload on the joints, especially the knees (repeated pivot movements).

Another remarkable finding is that the swimming team had significantly lower CTX-II concentrations compared with the control group (►**Fig. 5**). In other words, swimming was a protective factor for the articular collagen in the investigated

population. This finding is likely due to a combination of factors known to protect the joints, including aerobic exercise, low-impact activity and strengthening of the periarticular muscles.[17]

Conclusion

Therefore, we conclude that, in the investigated population, professional *futsal* training is a risk factor for type-II collagen degradation and, thus, for articular cartilage degradation. In contrast, swimming is a protective factor for the joints in this same population, resulting in less articular collagen degradation.

Such data suggests that some sports can indeed lead to early articular degradation. Sports trauma physicians must consider this fact, and clinical protocols aimed at joint protection must be studied and applied.

However, the findings of the present study indicate that some sports may provide joint protection, suggesting an important tool to prevent joint erosion, and mixed training may be highly beneficial for professional teams.

Further studies on this subject must be performed with larger samples, and they should be aimed at controlling articular destruction using pharmacological and non-pharmacological means.

In addition, the use of biomarkers of joint destruction is an important tool for the early detection of joint overload. Those working in sports trauma need to diagnose joint lesions early to improve the lives of athletes.

Conflicts of Interest
The authors have none to declare.

References

1 Martel-Pelletier J, Boileau C, Pelletier JP, Roughley PJ. Cartilage in normal and osteoarthritis conditions. Best Pract Res Clin Rheumatol 2008;22(02):351–384
2 Yoshimura M, Sakamoto K, Tsuruta A, et al. Evaluation of the effect of glucosamine administration on biomarkers for cartilage and bone metabolism in soccer players. Int J Mol Med 2009;24(04): 487–494
3 Arokoski JP, Hyttinen MM, Lapveteläinen T, et al. Decreased birefringence of the superficial zone collagen network in the canine knee (stifle) articular cartilage after long distance running training, detected by quantitative polarised light microscopy. Ann Rheum Dis 1996;55(04):253–264
4 Arokoski J, Jurvelin J, Kiviranta I, Tammi M, Helminen HJ. Softening of the lateral condyle articular cartilage in the canine knee joint after long distance (up to 40 km/day) running training lasting one year. Int J Sports Med 1994;15(05):254–260
5 Arokoski JP, Jurvelin JS, Väätäinen U, Helminen HJ. Normal and pathological adaptations of articular cartilage to joint loading. Scand J Med Sci Sports 2000;10(04):186–198
6 Arokoski J, Kiviranta I, Jurvelin J, Tammi M, Helminen HJ. Long-distance running causes site-dependent decrease of cartilage glycosaminoglycan content in the knee joints of beagle dogs. Arthritis Rheum 1993;36(10):1451–1459
7 Buckwalter JA. Evidence for overuse/overloading of joints in the genesis and progression of osteoarthritis. Curr Orthop 1996;10 (04):220–224
8 Buckwalter JA, Martin JA. Sports and osteoarthritis. Curr Opin Rheumatol 2004;16(05):634–639
9 Coimbra IB, Pastor EH, Greve JM, Puccinelli ML, Fuller R, Cavalcanti FS. Consenso brasileiro para o tratamento da osteoartrite (artrose). [Brazilian consensus for treatment of osteoarthritis (arthrosis)]Rev Bras Reumatol 2002;42(06):371–374
10 Dye SF. The pathophysiology of patellofemoral pain: a tissue homeostasis perspective. Clin Orthop Relat Res 2005;426(436): 100–110
11 Hilliquin P. Le Sport chez l'arthrosique. Rev Rhum 2007;74:587–591
12 Luepongsak N, Amin S, Krebs DE, McGibbon CA, Felson D. The contribution of type of daily activity to loading across the hip and knee joints in the elderly. Osteoarthritis Cartilage 2002;10(05): 353–359
13 Oettmeier R, Arakoski J, Roth AJ. Subchondral bone and articular cartilage responses to long distance running training (40 km per day) in the beagle knee joint. Eur J Exp Musculoskel Res. 1992;1:145–154
14 Rezende UM, Gobbi RG. Tratamento medicamentoso da osteoartrose do joelho. Rev Bras Ortop 2009;44(01):14–19
15 Rolland Y, Glisezinski I, Crampes F, Pillard F, Rivière D. Sports et arthrose fémorotibiale. Sci Sports 2000;15:125–132
16 Venn MF. Chemical composition of human femoral and head cartilage: influence of topographical position and fibrillation. Ann Rheum Dis 1979;38(01):57–62
17 Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008;16(02):137–162
18 Rodeo SA, Hidaka C, Maher SA. What's new in orthopaedic research. J Bone Joint Surg Am 2005;87(10):2356–2365
19 Bruyere O, Collette J, Kothari M, et al. Osteoarthritis, magnetic resonance imaging, and biochemical markers: a one year prospective study. Ann Rheum Dis 2006;65(08):1050–1054
20 Conrozier T, Balblanc JC, Richette P, et al; Osteoarthritis Group of the French Society of Rheumatology. Early effect of hyaluronic acid intra-articular injections on serum and urine biomarkers in patients with knee osteoarthritis: An open-label observational prospective study. J Orthop Res 2012;30(05): 679–685
21 Dam EB, Loog M, Christiansen C, et al. Identification of progressors in osteoarthritis by combining biochemical and MRI-based markers. Arthritis Res Ther 2009;11(04):R115
22 Duclos ME, Roualdes O, Cararo R, Rousseau JC, Roger T, Hartmann DJ. Significance of the serum CTX-II level in an osteoarthritis animal model: a 5-month longitudinal study. Osteoarthritis Cartilage 2010;18(11):1467–1476
23 Felson DT, Lohmander LS. Whither osteoarthritis biomarkers? Osteoarthritis Cartilage 2009;17(04):419–422
24 Huebner JL, Kraus VB. Assessment of the utility of biomarkers of osteoarthritis in the guinea pig. Osteoarthritis Cartilage 2006;14 (09):923–930
25 Ishijima M, Watari T, Naito K, et al. Relationships between biomarkers of cartilage, bone, synovial metabolism and knee pain provide insights into the origins of pain in early knee osteoarthritis. Arthritis Res Ther 2011;13(01):R22
26 Karsdal MA, Byrjalsen I, Bay-Jensen AC, Henriksen K, Riis BJ, Christiansen C. Biochemical markers identify influences on bone and cartilage degradation in osteoarthritis–the effect of sex, Kellgren-Lawrence (KL) score, body mass index (BMI), oral salmon calcitonin (sCT) treatment and diurnal variation. BMC Musculoskelet Disord 2010;11:125
27 Mazières B, Garnero P, Guéguen A, et al. Molecular markers of cartilage breakdown and synovitis at baseline as predictors of structural progression of hip osteoarthritis. The ECHODIAH Cohort. Ann Rheum Dis 2006;65(03):354–359
28 Sowers MF, Karvonen-Gutierrez CA, Yosef M, et al. Longitudinal changes of serum COMP and urinary CTX-II predict X-ray defined knee osteoarthritis severity and stiffness in women. Osteoarthritis Cartilage 2009;17(12):1609–1614