

# Impact of collagen hydrolysate in middle-aged athletes with knee and ankle osteochondral lesions: A case series

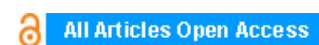
**Fábio Krebs Gonçalves**

## ABSTRACT

**Introduction:** Osteochondral lesions (OCL) are a significant issue among professional and amateur athletes in several sports modalities. Lack of treatment or inadequate therapy may aggravate the symptoms and jeopardize the chance of a complete functional recovery. Multidisciplinary treatment is the mainstay of OCL, including physiotherapy, physical rehabilitation with aerobic and anaerobic exercises and lately, the use of nutritional supplementation with collagen hydrolysate (CH).

**Case Series:** We report three cases of OCL in athletes, which were diagnosed and followed with magnetic resonance imaging (MRI) scan after multidisciplinary treatment including nutritional supplementation with Fortigel® a specific collagen hydrolysate that contains bioactive collagen peptides. A literature review on the role of collagen hydrolysate and its nutritional aspect in supporting the regeneration of articular cartilage is also presented.

**Conclusion:** MRI images of patients assessed in this study depict the recovery of the articular surfaces after the treatment. Also, studies in athletes presenting joint pain but otherwise not diagnosed with osteoarthritis or other osteoarticular diseases have demonstrated the beneficial effects of CH intake.



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**Keywords:** Athletes, Collagen hydrolysate, Nutritional supplementation, Osteochondral lesions

### How to cite this article

Gonçalves FK. Impact of collagen hydrolysate in middle-aged athletes with knee and ankle osteochondral lesions: A case series. Int J Case Rep Images 2017;8(6):364–369.

Article ID: Z01201706CS10087FG

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doi:Z01201706CS10087FG

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Received: 23 January 2017

Accepted: 10 March 2017

Published: 01 June 2017

## INTRODUCTION

Osteochondral lesions (OCL) are a significant issue among professional and amateur athletes in several sports modalities. Lack of treatment or inadequate therapy may worsen the symptoms and jeopardize the chance of a complete functional recovery. Osteochondral lesions can be induced by several factors, such as ischemia, repetitive microtrauma and acute trauma. These lesions may affect any joint, but they are most commonly seen in the weight-bearing area of the lateral femoral condyle, the inferomedial pole of the patella and the talar dome [1].

Multidisciplinary treatment is the mainstay of OCL, despite being surgical or conservative. It involves physiotherapy, physical rehabilitation with aerobic and anaerobic exercises and lately, the use of nutritional supplementation with collagen hydrolysate.

Collagen is the main insoluble fibrous protein in the extracellular matrix and is commonly found in the skin, tendons, cartilage, bone and cornea. This complex protein consists of repeated amino-acid sequences (especially glycine, proline and hydroxyproline) packed together and forming fibrils [2, 3]. There are over 20 known different types of collagen, but types I, II and III comprise about 90% of what is found in the human body.

Type II collagen is the principal protein found in cartilage, and its small fibrils disposed in a random fashion on the proteoglycan matrix confer traits of strength and compressibility that allows absorption of impacts [2, 3]. There are four distinct zones (superficial, transitional, deep and calcified) found in the articular cartilage, which are defined by the morphological differences in density, cellular disposition (chondrocytes), nature, content and distribution of proteoglycans and the special organization of the collagen fibrils. The percentage of collagen found in the superficial layers of the articular cartilage reaches 80%, while the deeper layers have around 65% of that protein in their structure [4].

Sanctioned as a safe food ingredient by regulatory agencies, collagen hydrolysate is obtained by enzymatic hydrolysis of animal collagenous tissues (mainly skin) and has an identical amino acid composition to type II collagen with high levels of glycine and proline, which are a prerequisite for a healthy cartilage [5–7].

We aim to report three cases of OCL in athletes, which were diagnosed and followed with magnetic resonance imaging (MRI) scan after multidisciplinary treatment that included nutritional supplementation with Fortigel®, a specific collagen hydrolysate, developed by Gelita Company (Heidelberg, Germany), which contains bioactive collagen peptides (BCP). A literature review on the role of collagen hydrolysate in supporting the benefits from a specific nutritional approach focused on cartilage is also presented.

## CASE SERIES

### Case 1

A 42-year-old male farmer, who plays seven-a-side indoor soccer twice a week and jogs three times a week. He sought medical attention due to pain in the right knee and difficulty in walking following a sprain whilst playing indoor soccer. Patient's body measurements were as follows: 1.75 m, 70 kg and 22.86 kg/m<sup>2</sup> of body mass index (BMI). Physical examination showed neutral alignment of lower limbs, pain on the medial joint line and medial femoral condyle during palpation. Limitation of final knee flexion and pain during the McMurray test for the medial meniscus were also detected. All ligament tests were normal, with motion ranges of 0–140 degrees on left knee and 0–115° on the right one. An MRI of the right knee performed a month after his lesion showed deep ulceration on the medial femoral condyle's weight-

bearing cartilage, area with intense reactional bone edema in the spongy section of the femoral condyle, slight strain on the medial collateral ligament, and edema on adjacent soft tissues (Figure 1A).

Final diagnosis was right knee pain due to osteochondral ulceration on the medial femoral condyle. Treatment included physiotherapy and the daily oral intake of 10 grams of collagen hydrolysate Fortigel® dissolved in a glass of water. The patient returned six months later, having undergone 20 sessions of physiotherapy and reporting significant pain reduction. He was counseled to maintain the physiotherapy program, continue the intake of collagen hydrolysate and initiate physical activities to ensure muscle strengthening. In his following consultation, after nine months, the patient was asymptomatic. Physical examination showed a slight weight loss (67 kg), absence of pain, edema or effusion on the joints, and normal range of mobility (0–140°) in both knees. A follow-up MRI scan performed 17 months after his lesion (Figure 1B) showed small, superficial chondral erosions on the medial femoral condyle's weight-bearing area with significant reduction of the ulcerations formerly detected and without reactional subchondral osteitis.

The patient was advised to maintain the ingestion of the collagen hydrolysate Fortigel® and continue with the physical training in the local academy, once-a-week soccer and treadmill running three times a week. With the subsequent functional recovery achieved, the patient was cleared to fully return to his sports practice while maintaining the therapeutic measures prescribed.

### Case 2

A 43-year-old salesman, who plays indoor soccer and runs twice a week. He suffered a sprained ankle during a soccer game. The attending physician ordered an X-ray

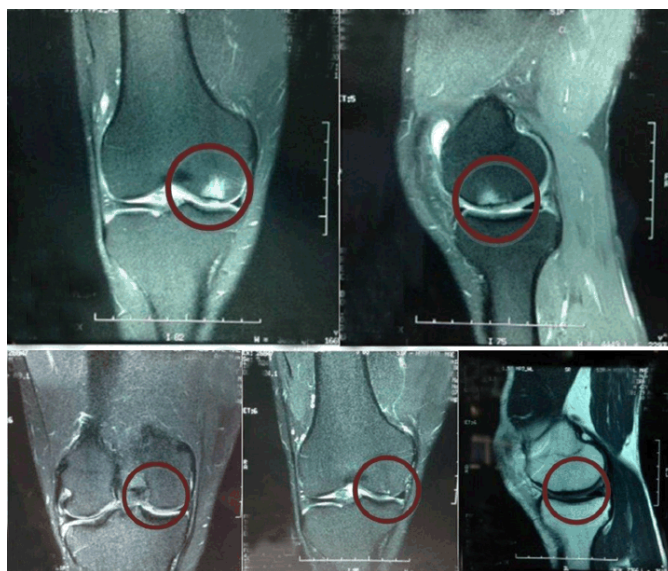


Figure 1: (A) Note deep ulceration on the medial femoral condyle's weight-bearing cartilage area (MRI 07/29/2013), (B) Note significant reduction of chondral erosions on the medial femoral condyle's weight-bearing area (MRI 11/10/2014).



that showed soft tissue edema on the periarticular area with no evidence of fractures or other bone lesions. The patient had the left ankle immobilized for 8 days and was prescribed non-steroidal anti-inflammatory drugs (NSAID). He came to a consultation almost a month after the lesion, reporting persisting ankle pains and difficulty to stand-up. Physical examination showed neutral alignment of lower limbs, edema and pain to the touch of the anterolateral surface of the left ankle. Mobility tests showed limitations on the left ankle with apparent ligament stability. Range of motion for plantar flexion was  $50^{\circ}$  on the right ankle and  $35^{\circ}$  on the left and for dorsiflexion  $12^{\circ}$  and  $4^{\circ}$  respectively. Patient's body measurements were 1.81 m, 80 kg and BMI of 24.42  $\text{kg}/\text{m}^2$ . He was diagnosed with a left ankle sprain with ligament lesion and prescribed the use of removable cast walker boots, as well as 20 sessions of physiotherapy. After concluding the treatment, the patient returned to his usual sports practice (indoor soccer and running). The patient was treated with removable immobilization and physical therapy and in a consultation, six years after his lesion, he informed recurring pains on the left ankle after exercising, with subsequent limitation of mobility. Physical examination showed pain during palpation of the anterior surface of the left ankle on the region of the tibiotalar joint. Mobility ranges for plantar flexion were  $50^{\circ}$  on the right ankle and  $30^{\circ}$  on the left one and dorsiflexion ranges were  $12^{\circ}$  and  $4^{\circ}$ , respectively. The MRI scan ordered on this consultation (Figure 2A) showed a significant osteochondral lesion on the medial talar dome with a strain on the anterior talofibular ligament. The patient was then recommended the daily oral intake of 10 g collagen hydrolysate (Fortigel®), advised to avoid high-impact activities and referred to the physiotherapist for treatment. On his next consultation, after 16 months, the patient reported to be pain-free. Physical examination showed a  $50^{\circ}$  plantar flexion on the right ankle and  $45^{\circ}$  on the left one, while dorsiflexion ranges were  $12^{\circ}$  and  $10^{\circ}$  respectively. Palpation on the anterior region of the left ankle was normal. A new MRI scan, conducted on the same period, showed preservation of the articular surface, without progression of the OCL on the talar dome or signs of instability (Figure 2B). Due to his functional recovery, the patient was advised to maintain the oral intake of the collagen hydrolysate Fortigel®, continue with physical training in the academy, start jogging and progressively return to running.

### Case 3

A 30-year-old male civil engineer, and a professional yachting (soling class) athlete. He sought medical attention reporting pain on the right knee following a game of padel tennis and sailing. He also complained of discomfort while walking and ascending/descending stairs. Physical examination showed neutral alignment of lower limbs, pain and crepitation during mobilization of the femoropatellar joint. Ligament and meniscal tests were normal. Flexion motion ranges were  $130^{\circ}$  on the right

knee and  $145^{\circ}$  on the left one. Extension was complete bilaterally. Patient's body measurements were 1.81 m, 80 kg and BMI of 24.69  $\text{kg}/\text{m}^2$ . An MRI scan of the right knee performed on the same day of his medical consultation showed patellar chondropathy with chondral fissures in the apex and medial facet, reaching into the deeper layers (Figure 3A). The images demonstrated stress areas on



Figure 2: (A) Note significant Osteochondral lesions on the medial talar dome with strain on the anterior talofibular ligament (MRI 07/30/2013), (B) Note preservation of the articular surface, without progression of the Osteochondral on the talar dome (MRI 11/12/2014).

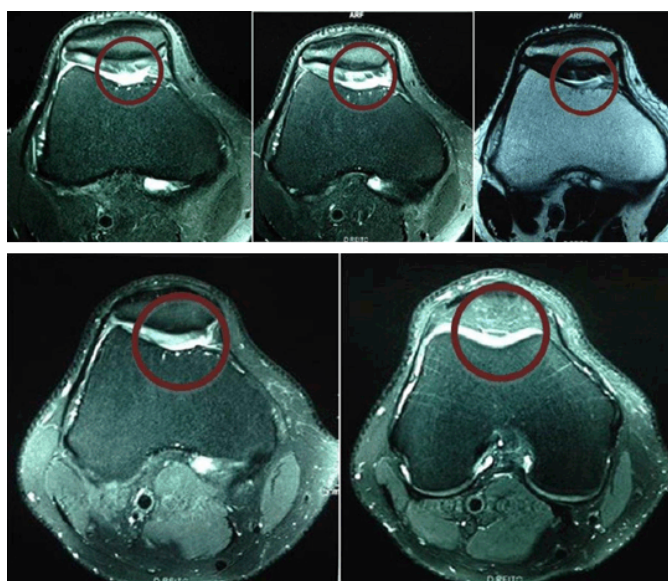


Figure 3: (A) Note the patellar chondropathy with chondral fissures in the apex and medial facet, reaching into the deeper layers (MRI 10/01/2014), (B) Note reduction of the OCL on the apex and medial facets and patellar ridge, reaching the superficial layers (MRI 01/16/2015).

the subchondral structures of the facets and the patellar ridge. Final diagnosis was knee pain due to patellar chondropathy. Treatment included daily oral intake of 10 g collagen hydrolysate (Fortigel®), physiotherapy and interruption of high-impact activities (such as sailing). On his return one month later the patient reported improvement of symptoms and decrease in the right knee pain. This patient presented a clinical and radiological picture indicative of osteochondral pathology at the level of the left ankle and a sequela of sprain with joint trauma, which caused him to withdraw from soccer practice and from races. He presented limitation of the joint mobility of the affected ankle, which recovered after interdisciplinary treatment and use of bioactive collagen peptide. With the functional recovery obtained clinically and radiologically, he was able to return to the partial progressive practice of his sports activities, with orientation to maintain the prescribed therapeutic measures. He was counseled to maintain the intake of collagen hydrolysate and re-initiate his training program since he would participate on an International Yachting Event (Soling Class) in one month. On his next consultation, after two months, the patient reported being asymptomatic and pain-free and also that he had been classified among the first six finalists on the yachting event. Physical examination showed normal mobility range on both knees, with 145° flexion and complete bilateral extension. A new MRI scan, performed on the same period, revealed signs of patellar chondropathy on the apex and medial facet, reaching only the superficial layers (Figure 3B). The exam showed reduction of the OCL on the facets and patellar ridge, in comparison to the previous one. The patient was advised to continue the use of the collagen hydrolysate Fortigel®, maintain his anaerobic activities (such as weight lifting) and also the aerobic training. The clinical and radiologic functional recovery allowed the patient to keep his sports activities and he became champion of the local boat race (XXI Copa da Cidade de Porto Alegre) in March 2015.

## DISCUSSION

The use of collagen hydrolysate as a nutraceutical or nutritional supplement has been studied on the last decades, not only for skin and hair diseases, but also in researches focusing on degenerative conditions of the musculoskeletal system, including nutritional aspects and in particular on joint cartilage health. Chondrocytes control the maintenance of the extracellular matrix and consequently the functional integrity of the articular cartilage. These cells are continuously placed in a dynamic mechanical environment, combining compression, variations in hydrostatic pressure and tension, which create a host of signals transmitted through the extracellular and pericellular matrixes and result in altered gene expressions and changing metabolism [8].

In vitro studies have shown that the addition of collagen hydrolysate in the culture medium of

chondrocytes increased the secretion of type II collagen in a dose-dependent fashion, suggesting a likely feedback mechanism to regulate the collagen turnover in cartilage tissue [9]. Chondrocytes also responded to collagen hydrolysate addition with a significant increase in proteoglycan synthesis, aggrecan expression and 1.5 fold increment in type II collagen biosynthesis [10].

Previous analysis of radiolabeled collagen hydrolysate determined that the orally administered substance was absorbed from the intestine and accumulated preferentially on the cartilage tissue [11]. A randomized placebo control study on animal osteoarthritis (OA) model demonstrated that the oral ingestion of collagen hydrolysate over a Three-month period led to a significant decrease in cartilage tissue degeneration in the knee joints when compared with non-treated subjects [12].

Clinical studies also pointed to a beneficial effect of collagen hydrolysate in patients with osteoarthritis of the knee and hip, with significant reduction in the consumption of analgesics after two months of intake [13]. Recently, Kumar et al. published a randomized, double blind, placebo controlled trial evaluating the effects of daily ingestion of 5 g collagen hydrolysate (two types) on the control of knee osteoarthritis in 30 patients [14]. The endpoints were measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), used to assess pain, stiffness, and physical function in patients with hip and/or knee osteoarthritis; a visual analog scale (VAS) and quality-of-life (QoL) parameters. Patients in the collagen hydrolysate group presented a statistically significant improvement in all endpoints ( $p < 0.01$ ) compared with those in the placebo arm.

Articular traumas are everyday occurrences among professional and recreational sports players. Several studies reported the prevalence of injuries among amateur athletes in various modalities. A prospective study with 231 amateur soccer players recorded 213 injuries (79% due to trauma) in 57% of the players during one season. Knee (20.2%) and ankle (19.2%) were often affected sites with strain and/or ligament lesions in 11.3% and 17.3%, respectively [15]. A retrospective analysis of 123 recreational athletes in several activities found that 74% reported injuries due to soccer practice (indoor, futsal, sand, and turf) [16]. Ankle sprains responded to almost half (49%) of the injuries in this study.

Sailing related injuries were surveyed, among others, by Fontoura and Oliveira, who reported 18.8% of foot and ankle lesions and 16.36% of knee traumas among 165 subjects and Moraes, who revealed that up to 32% of sailors in the Brazilian Olympic Team had knee pain [17, 18].

In fact, physical activity itself directly affects cartilage metabolism, as seen by the imbalance of proteoglycan degradation versus synthesis in the extracellular matrix after joint immobilization or by the direct damaging effects of overtraining [6].

We presented the case reports of three healthy athletes, two of them amateurs and one professional, engaged in



a wide range of sports practice (indoor soccer, running, padel tennis and sailing) that sought medical attention due to painful exercise-related osteoarticular lesions.

Studies in athletes presenting joint pain but otherwise not diagnosed with osteoarthritis or other osteoarticular diseases have demonstrated the beneficial effects of daily collagen hydrolysate oral intake.

An observational trial including one hundred athletes with exercise-related joint pain analyzed the effect of 10 g daily oral intake of collagen hydrolysate for 12 weeks on pain reduction [19]. The results showed that 78% of subjects reported reduction in pain levels on movement at the end of the observation period. Objective decrease in pain levels, measured on a 1–10 scale, was also confirmed by the attending physician.

A 24-week prospective, randomized, placebo-controlled, double blind study was conducted with 147 healthy college athletes complaining of arthralgia [20]. The students were randomized to receive either placebo or 10 g of collagen hydrolysate daily for the duration of the study. The level of pain on each joint at rest and during movement was recorded by students and physicians through a VAS in five visits. Data available for 97 subjects showed statistically significant changes in joint pain for the treatment group in six parameters: at rest recorded by the physician and by the subject ( $p = 0.025$  and  $p = 0.039$ , respectively), when walking ( $p = 0.007$ ), when standing ( $p = 0.011$ ), when carrying objects ( $p = 0.014$ ) and when lifting ( $p = 0.018$ ).

All the cases reported in the present paper were followed with MRI scan, documenting the improvement or stabilization of the OCL after the physiotherapy treatment and collagen hydrolysate supplementation. Magnetic resonance imaging (MRI) scan has been increasingly used to confirm the diagnosis, define the stages and document the evolution of OCL [21, 22]. The reliability of the method to recognize cartilage changes after collagen hydrolysate (Fortigel®) intake was demonstrated by McAlindon [23]. A single center, prospective, randomized, placebo-controlled, double blind trial included 30 patients with mild knee osteoarthritis, whose cartilage changes were followed by two MRI techniques (delayed gadolinium enhanced magnetic resonance imaging of cartilage - dGEMRIC or T2 mapping) before and after collagen hydrolysate nutritional supplementation. Results of this pilot trial showed an increase in the dGEMRIC score in two regions of interest in patients on the collagen hydrolysate group, suggesting an increment in the proteoglycan content in the cartilage. The results in the placebo group presented a decrease of the score on these regions.

Magnetic resonance imaging scan of our patients clearly represent the recovery of the articular surfaces after the treatment. Of course, case reports or series do not possess the adequate design to confirm hypotheses, and large, controlled, randomized trials would be necessary to measure how much of such recovery is due to the intake of collagen hydrolysate. However, the collecting of data and

the recording of evidence are fundamental to increase the body of knowledge on the treatment of OCL.

## CONCLUSION

The beneficial effects of collagen hydrolysate intake was observed in the series of the three cases reported in our study and is also demonstrated in several studies in athletes presenting joint pain but otherwise not diagnosed with osteoarthritis or other osteoarticular diseases. As more information becomes available on the nutritional effects of collagen hydrolysate in osteoarticular recovery and maintenance, we will likely have a broader range of tools at hand to ensure the best possible treatment to injured athletes.

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## Acknowledgements

We would like to thank Evidências, a Kantar Health company, for the editorial support in this paper.

## Author Contribution

Fábio Krebs Gonçalves – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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