Genç et al. BMC Musculoskeletal Disorders (2025) 26:17
https://doi.org/10.1186/s12891-024-08244-w

BMC Musculoskeletal Disorders

RESEARCH

Open Access

The effect of supplementation with type I and type III collagen peptide and type II hydrolyzed collagen on pain, quality of life and physical function in patients with meniscopathy: a randomized, double-blind, placebo-controlled study

Ahmet Serhat Genç[1], Ali Kerim Yılmaz[2*], Berna Anıl[2], Esra Korkmaz Salkılıç[2], Enes Akdemir[2], Berna Güzel[3], Ahmet Mor[4], Hacı Ahmet Yarar[5], Nizamettin Güzel[6] and Lokman Kehribar[6]

Abstract

Background Menisci, one of the most important anatomical structures of the knee joint, plays a role in load transfer, stability, shock absorption, prevention of articular cartilage degeneration, and proprioception. Type I collagen, the main component of the meniscus, and type II collagen fibers play an important role in the stability of the knee joint. This study aimed to evaluate the effects of Naturagen® 4 Joint product containing type I, II, and III collagen on pain, quality of life, and physical functions in patients with meniscopathy.

Methods This randomized, double-blind, placebo-controlled clinical study included 32 patients (collagen = 17 and placebo = 15) with meniscopathy. Patients completed the Visual Analog Scale (VAS), Western Ontario and McMaster Universities Osteoarthrtis Index (WOMAC), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Oxford Knee Score (OKS), Tampa Scale for Kinesiophobia (TSK), Short Form Health Survey (SF-12), Lower Extremity Functional Scale (LEFS), Foot Function Index (FFI), proprioceptive sensation, Timed Up and Go (TUG), 6-Minute Walking Test (6MWT), The Five Repetition Sit to Stand Test (5STS), Stair Climbing Test (SCT), Berg Balance Scale (BBS) and back and leg strength tests and scales were applied. All tests were repeated before and after eight weeks of collagen supplementation.

Results The study showed that eight weeks of supplementation with various collagen types had statistically significant effects on pain, quality of life, kinesiophobia, and foot function scale scores in patients with meniscopathy ($p < 0.05$). Similarly, eight weeks of supplementation showed a statistically significant difference in leg strength ($p = 0.057$), but no significant difference was found in back strength, proprioception, balance, and various functional test results ($p > 0.05$).

*Correspondence:
Ali Kerim Yılmaz
akerim.yilmaz@omu.edu.tr
Full list of author information is available at the end of the article

Conclusions The results of the study showed that the eight-week collagen-based supplement had a positive effect on pain and quality of life levels and some functional test results in patients with meniscopathy. Longer-term studies and diversification of subject groups will help to understand better the effects of the product on meniscal tears and symptoms.

Trial registration The study was retrospectively registered in the Iranian Clinical Trials Registry on 14/05/2024 with the number IRCT20240411061470N2.

Keywords Meniscal tear, Collagen supplement, Pain, Physical function, Quality of life

Introduction

Menisci, one of the most important anatomical structures of the knee joint, are fibrocartilaginous tissues that act through interactions between the femur, tibia and patella [1]. Ligaments provide knee stability, articular cartilage reduces friction, and menisci play a role in load distribution, shock absorption, prevention of articular cartilage degeneration and proprioception [2]. The capacity to resist the forces applied to the knee is related to the biomechanical properties of the meniscus tissue and prevents overstretching and possible injury of the knee, especially in movements requiring high effort such as running, jumping and carrying heavy loads [2, 3]. However, the knee joint performs its movement in more than one plane and is therefore susceptible to injuries [2]. Meniscal tears may occur as a result of these injuries. These tears, which are characterized by slow healing, occur mostly in the avascular region [4]. Meniscal tears usually occur as a result of trauma in young people but may also occur without trauma in the elderly due to meniscal degeneration and decreased elasticity [5].

After a meniscal tear, the menisci cannot perform their normal functions, and the biomechanics of the knee joint deteriorate. In addition, the functional performance of the individual decreases with symptoms such as locking, effusion, and recurrent pain in the knee; daily life is restricted, and quality of life is significantly affected [6]. When conservative methods used to treat meniscal tears (nonoperative rehabilitation, nonsteroidal anti-inflammatory drugs, and intra-articular injections) become insufficient to relieve these symptoms, surgical methods such as meniscal repair, meniscectomy, meniscal allograft transplantation and the use of meniscal scaffolds are used [3, 7]. According to the three-grade staging system currently used in meniscal injuries, most of the grade 1 and 2 injuries are treated conservatively, whereas arthroscopic surgery or excision is preferred in grade 3 injuries [8, 9]. Meniscectomy, which is based on the procedure of removing the damaged tissue, is one of the traditional and common methods in the treatment of meniscal tears [10, 11]. However, both partial and total meniscectomy are known to lead to degeneration and osteoarthritis in the knee joint due to increased cartilage contact stress [10, 12]. As a result of such limitations after intervention, orthopedists have turned to various treatment methods to preserve meniscal function in the process [7, 13–15]. Studies have shown that strengthening exercises may be as effective as arthroscopic surgery in relieving knee pain, improving knee function, and increasing patient satisfaction in degenerative horizontal tears of the meniscus [16–18]. In addition, the importance of considering non-surgical approaches, including rehabilitation and physical exercise, as the first line of treatment in asymptomatic meniscal injuries has been emphasized [18, 19].

The meniscal content is highly hydrated (72% water) [3, 20]. The remaining content consists of extracellular matrix and cells. The organic matter consists mainly of collagen (75%), glycosaminoglycans (17%), DNA (2%), adhesion glycoproteins (< 1%), and elastin (< 1%) [3, 20]. Along with type I collagen, which is the main component of the meniscus, type II collagen fibers play an important role in the stability of the knee joint by showing the ability to withstand the stresses exposed [10, 21, 22]. It is said that a collagen matrix must be formed for the deposition of glycosaminoglycans that contribute to the compression properties of the meniscus [23]. Collagen plays a vital role in joint health and cartilage formation and is highly effective in preventing joint pain and progressive cartilage damage over time [24, 25]. In addition, it is thought that collagen supplementation may help the treatment of knee injuries with its positive effects on healing and symptom reduction [26]. Many studies have shown that collagen supplementation is effective in treating degenerative joint disorders and reduces pain symptoms [27–30].

There are many studies on knee joint injuries in the literature. Although meniscal tears are one of the most common orthopedic injuries of the knee, there are limited studies on the effect of collagen supplementation on meniscal tears and symptoms. In this context, our study aims to examine the effects of type I and type III collagen peptide and type II hydrolyzed collagen component supplementation on pain, quality of life, and physical functions associated with meniscal tears.

Material and method

Investigational products

The study product was provided by Naturagen® 4 Joint Naturagen İlaç Kozmetik AŞ, Turkey, registered with the US Food and Drug Administration (Registration No: 12537420128). The product contained 15 stick sachets of 5.75 g in a box. Naturagen® 4 Joint contained varying amounts of PROFIN® bovine collagen peptides (type I and type III), glucosamine sulfate, chondroitin sulfate, methylsulfonylmethane, malic acid, lemon flavoring, calcium l-ascorbate, hyaluronic acid, maltodextrin, olibanum gum resin extract, chicken hydrolyzed collagen (type II), silicon dioxide, steviol glycosides and vitamin C. The ingredient profile of the product is shown in Table 1. The placebo product contained 5.2 g maltodextrin. Both products contained sweeteners with the same flavor. All products had the same appearance, taste, and texture.

Table 1 Product ingredients and daily doses

Ingredients	Daily intake dose per sachet
Collagen peptides (Type I, III)	2000 mg
Glucosamine sulfate	1500 mg
Chondroitin sulfate	750 mg
Methylsulfonylmethane	500 mg
Hyaluronic acid	100 mg
Olibanum Gumresin Extract	50 mg
Hydrolyzed Collagen (Type II)	40 mg
Vitamin C	100 mg

Study design

This randomized, double-blind, placebo-controlled clinical trial evaluated the effects of eight weeks of use of Naturagen® 4 Joint product with a combination of type I and type III collagen peptide and type II hydrolyzed collagen, glucosamine sulfate, chondroitin sulfate, hyaluronic acid, and vitamin C on various pain and quality of life scales, balance and various functional test results in meniscopathy patients. The study included 32 patients who completed written informed consent forms (Fig. 1). In addition to descriptive information and limb lengths, Western Ontario and McMaster Universities Osteoarthrtis Index (WOMAC), Visual Analog Scale (VAS), Oxford Knee Score (OKS), Foot Function Index (FFI) and Berg Balance Scale (BBS) scales, 6-Minute Walking

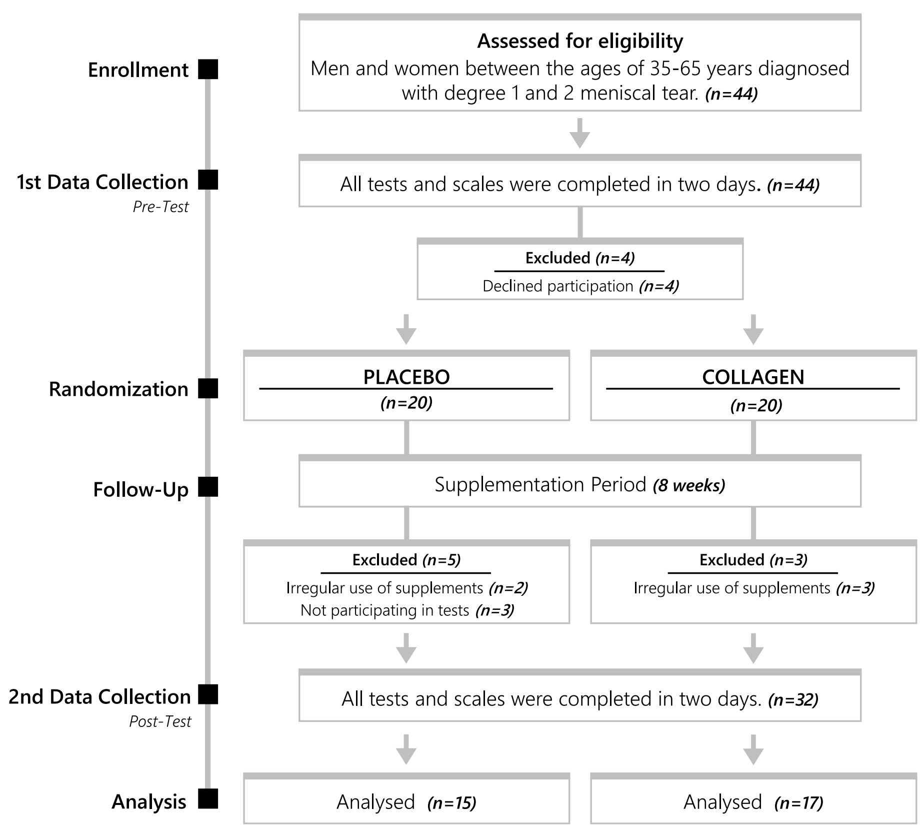

Fig. 1 Flowchart

Test (6MWT), The Five Repetition Sit to Stand Test (5STS) and proprioception measurements were taken at their first visit. On the day following the first visit, Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Tampa Scale for Kinesiophobia (TSK), Short Form Health Survey (SF-12), and Lower Extremity Functional Scale (LEFS) scales, Timed Up and Go (TUG), Stair-Climbing Test (SCT), back and leg strength tests were performed. After completion of the pre-tests, participants were randomized to one of the two treatment groups using computer-certified software (www.random.org) and divided into collagen ($n=17$) and placebo ($n=15$) groups. Blinding of the products was done using blinding codes in sealed envelopes. Participants and the investigators responsible for data collection were blinded to treatment allocation. Participants were instructed to consume the products according to the manufacturer's recommendation, one sachet per day, dissolved in one glass (200 ml) of water, for eight weeks. For a better follow-up process, participants were assigned diary cards, and their product use was recorded in this way. Participants continued their usual rehabilitation programme throughout the study. They were also asked to keep their general daily physical activity level and not to participate in any additional physical activity programme other than their ongoing rehabilitation during the study period. Participants returned after eight weeks of product use, and the post-tests were completed on two consecutive days in the same order as the pre-tests. All measurements in the study were performed at the same time of the day (13.00–15.00). The primary endpoint of the study was the successful completion of the final tests after eight weeks of product use, and the secondary endpoints were the patient's unwillingness to continue the study for various reasons, discontinuation of product use earlier than eight weeks, any additional trauma to the index joint, and the development of hypersensitivity to the product used in the study.

This study was conducted in compliance with the ethical principles stated in the Declaration of Helsinki and ICH Good Clinical Practice guidelines. Ethics committee approval was obtained from Sinop University Human Research Ethics Committee (protocol no: 2023/182) and registered in the Iranian Clinical Trials Registry on 14/05/2024 with the number IRCT20240411061470N2.

Participants

Thirty-two male and female subjects aged 35–65 years with grade 1 and 2 meniscal tears according to the three-grade staging system developed by Fischer et al. [9] participated in the study. G*Power 3.1 software was used to determine the number of subjects to participate in the study, and the results showed that it would be appropriate to conduct the study with 15 subjects in both groups (effect size r: 0.93, lower and upper critical p: 0.51, true power: 0.85). The inclusion and exclusion criteria for the subjects in the study are presented in Table 2.

Evaluation tools

Pain and quality of life scales

Visual Analogue Scale (VAS): It is used for knee pain assessment and the patient self-assesses [31]. It is a 100 mm scale. The patient marks the point on the line between 'no pain' and 'excruciating pain' according to their own pain level during free walking movement. A higher score means more pain.

Table 2 Inclusion and exclusion criteria for the study

Inclusion criteria
Diagnosis of unilateral or bilateral grade 1 or 2 meniscal tear
No history of any serious acute trauma to the knee
No X-ray or MRI evidence of osteoarthritis
ACL and other ligament structures are healthy according to MRI and Lachman test
Non-vegetarian
Willingness to participate in all visits and tests foreseen for the study
Exclusion criteria
Any history of trauma, fracture, or surgery on the index joint
Evidence or history of clinically significant hematologic, renal, endocrine, pulmonary, gastrointestinal, cardiovascular, hepatic, or neurologic diseases or malignancies within the last five years
Active viral or bacterial infection according to clinical examination
Knee surgery within the last 12 months or planned surgery within the working period
Intra-articular injections (cortisol, hyaluronic acid, etc.) within the last six months
Taking supplements such as hydrolyzed collagen, glucosamine, or chondroitin in the last six months
Intolerance to protein-based foods or supplements, pregnant or breastfeeding, and alcohol dependence

Western Ontario and McMaster Universities Osteoarthrtis Index (WOMAC): A 5-point Likert-type scale (none, mild, moderate, severe, extreme) consisting of 24 items and three subscales: pain, stiffness, and physical function. The scale is scored from 0 to 100, with a higher score indicating increased pain, stiffness, and functional limitations [32].

Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS): The KOOS-PS scale assesses activities of daily living and physical function after knee injuries [33]. The scale is scored on a 5-point Likert scale (none, mild, moderate, severe, extreme) and is evaluated between 0 and 100 points. A score of 0 indicates the absence of a problem, and a score of 100 indicates the severity of the knee problem.

Oxford Knee Score (OKS): The OKS assesses the patient's pain and functional status over the last four weeks and consists of 12 questions [34]. On a scale of 0 to 48, lower scores indicate worse pain and functional status.

Tampa Scale for Kinesiophobia (TSK): The scale, which covers fear of falling and fear of movement, has 17 questions scored between 1–4. Questions 4, 8, 12, and 16 are reversed. The highest score is 68. Higher scores indicate more fear of falling and movement in the patient [35].

Short Form Health Survey (SF-12): It is scored in two sub-dimensions: Physical Component Score (PCS) and Mental Component Score (MCS). Both subscales are scored between 0 and 100, with higher scores indicating better physical and mental health [36].

Lower Extremity Functional Scale (LEFS): The LEFS consists of 20 items assessing lower limb function and activity limitation [37]. Each item is scored between 0 and 4 on a scale of 'extremely difficult' to 'no difficulty,' with a maximum score of 80. High scores indicate a high functional level.

Foot Function Index (FFI): There are a total of 23 items on the scale, which is evaluated in the sub-dimensions of pain, disability, and activity limitation [38]. A higher score indicates more pain, disability, and activity limitation. All answers are summed and divided by the maximum score that can be obtained, and the total score is calculated by multiplying the number obtained by 100.

Functional tests

Back and leg force

For back strength measurement, feet were placed on the dynamometer stand. Knees and arms were stretched, the back was straight, and the trunk was slightly tilted forward; the dynamometer bar grasped with both hands was pulled vertically as best as possible with the back muscles active. For leg strength, they were asked to pull the bar in a vertical direction using only the leg until the knee was in extension with arms stretched, back straight, and trunk slightly tilted forward.

Proprioceptive sensory evaluation

Knee joint proprioceptive sensation was measured with a digital goniometer (2176–300 Insize Digital Angle Meter) with one degree of sensitivity. The goniometer was fixed to the patient's knee joint with EMG bandages. Then, 15°, 30°, 45°, and 60° angles were set as targets for evaluation. The goniometer was zeroed in the prone and supine positions with eyes closed, the patient's hips in a neutral position, both knees in full extension position, and the knee set to the target angle was verbally communicated to the patient. The patient then focused on the target angle for five seconds. Then, the patient positioned the knee to the target angle without external intervention. The mean angular errors of the measurements repeated three times for each angle were evaluated.

Timed up and go (TUG)

While seated in a standard chair, the patient was instructed first to stand up, walk three meters, and then turn around and sit back in the chair. The patient was able to use assistive devices such as a cane when necessary. The time until sitting again was recorded in seconds.

Six-minute walking test (6MWT)

A 30 m corridor was allocated for the Test. The patient was asked to walk in this corridor for six minutes. He was allowed to stop and rest when needed and to use assistive devices such as canes. When the time was over, the distance covered was recorded in meters.

The five repetition sit to stand test (5STS)

On a standard chair, the patient was asked to sit and stand once with his/her hands crossed over his/her chest. The Test was then initiated, and the patient was instructed to sit and stand on the chair five times as fast as possible. The time taken for five repetitions was recorded in seconds.

Stair-climbing test (SCT)

They were asked to ascend and descend a five-step ladder at a standard height for SCT as fast as possible. When necessary, they were allowed to hold on to the bars on the sides of the stairs, and the elapsed time was recorded in seconds.

Berg balance scale (BBS)

The scale consists of 14 questions that evaluate fall risk and loss of balance. Each item is scored between 0 and 4. The scores are evaluated as high fall risk (0–20), moderate fall risk (21–40), and low fall risk (41–56). A standard chair, a standard step, a 15-m corridor, and a stopwatch were used for the Test.

Statistical analysis

Data analyses were conducted using IBM SPSS Statistics version 22.0 (IBM Inc., Chicago, IL, USA). We represented our data using means and standard deviations. To check whether the data was normally distributed, we looked at histograms and conducted the Shapiro–Wilk test. Differences among groups were assessed using the One-Way ANOVA test. To compare groups over time, we employed a mixed repeated-measures analysis of variance (RM ANOVA), incorporating a Bonferroni correction for post hoc analyses. The study considered 'time' (pre- and post-measurements) and 'group' (placebo and collagen) as within-subject and between-subject factors, respectively. We tested for sphericity using Mauchly's Test. If this assumption was not met (indicated by $p<0.05$), we adjusted our approach using the Greenhouse–Geisser method. Another important aspect of our analysis was to examine the interaction between 'time' and 'group.' This interaction check helps understand if the effect of time varies across different groups. An interaction may suggest that time changes between groups may not be equivalent; however, no substantial violations were detected. All our statistical tests were two-tailed, and we set our threshold for statistical significance at $p<0.05$.

Results

In Table 3, the descriptive data of the groups are presented as mean ± standard deviation. There was no statistical difference between the placebo and collagen groups, and all parameters were similar ($p>0.05$).

Table 4 shows the pre and post-comparisons of pain, kinesiophobia, and quality of life scales in placebo and control groups. In the collagen group, VAS ($p=0.052$) and WOMAC Stiffness ($p=0.237$) parameters were not significant, while KOOS ($p=0.004$), OXFORD ($p=0.002$), TSK ($p=0.002$), SF-12 PCS ($p<0.001$), SF-12 MCS ($p=0.001$), LEFS ($p<0.001$) WOMAC Pain ($p<0.001$), WOMAC Physical function ($p<0.001$) and WOMAC TOTAL ($p<0.001$) scores showed a statistically significant difference and a positive result was observed. In the placebo group, no significant difference was found in any parameter ($p>0.05$).

In Table 5, knee proprioceptive sensation was evaluated pre- and post-in meniscopathy and contralateral sides in placebo and collagen groups. In the collagen group, statistically significant positive results were obtained on the contralateral side at 15 ($p=0.024$) and 30 degrees prone ($p=0.044$) and 15 ($p=0.007$) and 30 degrees supine ($p<0.001$). In the placebo group, significance was seen at 30 degrees supine on the contralateral side ($p<0.001$). In both groups, pre and post-evaluations of the meniscopathy side showed similar results ($p>0.05$).

Table 3 Descriptive data

	Placebo ($n=15$) *Mean ± SD*	Collagen ($n=17$) *Mean ± SD*
Characteristic		
Age (year)	43.1 ± 13.7	41.7 ± 8.2
Height (cm)	170.1 ± 6.8	165.1 ± 9.4
Weight (kg)	83.5 ± 16.2	76.9 ± 11
BMI (kg/m^2)	28.7 ± 4.2	28.3 ± 3.6
Gender		
Male	6 (40%)	6 (35%)
Female	9 (60%)	11 (65%)
Meniscopaty side		
Right	3 (20%)	6 (35%)
Left	12 (80%)	11 (65%)
Dominant side		
Right	14 (93%)	15 (88%)
Left	1 (7%)	2 (12%)

SD standard deviation, *BMI* body mass index

Figure 2 demonstrates that when the pain, activity limitation, and inability sub-dimensions of the Foot Function Index are evaluated pre- and post-intervention in the placebo and collagen groups, the collagen group showed statistically significant positive results. Specifically, there were significant improvements in the meniscopathy side AFI pain ($p=0.014$) and activity inability ($p=0.034$) sub-dimensions, as well as in the contralateral side AFI pain ($p=0.013$) and activity inability ($p=0.034$) sub-dimensions. The placebo group showed no statistically significant difference in AFI scores and similar results in meniscopathy and contralateral side pre and post-evaluations ($p>0.05$).

Figure 3 shows the pre- and post-comparisons of TUG, 6MWT, 5STS, SCT, and BBS and back and leg strength assessments in the placebo and collagen groups. Although there was a difference close to significance in leg strength in the collagen group, in general, pre and post-evaluations of all parameters in the collagen and placebo groups revealed similar results ($p>0.05$).

Discussion

This randomized, placebo-controlled study evaluated the effects of a newly developed supplement with a combination of type I and type III collagen peptide and type II hydrolyzed collagen, glucosamine sulfate, chondroitin sulfate, hyaluronic acid, and vitamin C on various pain and quality of life scales, balance, various functional test results, and strength levels in patients diagnosed with grade 1 and 2 meniscopathy according to the three-grade

Table 4 Intragroup and intergroup evaluation of pain, kinesiophobia, and quality of life scale results

	Placebo			Collagen					Interaction		
	Pre	Post		Pre	Post		Pre vs. Pre	Post vs. Post	Group	Time	Group x Time
	Mean ± SD	*Mean ± SD*	*p*	*Mean ± SD*	*Mean ± SD*	*p*	*p*	*p*	*p*	*p*	*p*
VAS	6.4 ± 2.3	5.6 ± 2.1	0.229	5.3 ± 3.3	4 ± 2.8	0.052	0.285	0.053	0.063	0.022*	0.780
KOOS-PS	11.7 ± 6.4	12.1 ± 4.4	0.829	11.8 ± 7.8	5.8 ± 6.3	0.004*	0.804	0.028*	0.204	0.013*	0.093
OKS	15.5 ± 6.6	13.3 ± 7.5	0.410	13.7 ± 8.1	5.8 ± 7.2	0.002*	0.659	0.018*	0.045*	0.001*	0.266
TSK	45.3 ± 6.3	41.7 ± 6.1	0.218	42.1 ± 7.8	33.2 ± 9.7	0.002*	0.051	0.014*	0.004*	0.007*	0.135
SF-12 PCS	37.9 ± 9.3	37.3 ± 7.7	0.835	38.3 ± 6.9	52.4 ± 7.8	< 0.001*	0.934	< 0.001*	0.011*	0.001*	0.001*
SF-12 MCS	44.3 ± 13	43.8 ± 12.4	0.862	41.4 ± 11.7	52.3 ± 7.8	0.001*	0.057	0.051	0.212	0.208	0.005*
LEFS	44.3 ± 13.7	44.4 ± 12.4	0.980	45.6 ± 18.3	68.5 ± 14.7	< 0.001*	0.954	0.001*	0.020*	0.001*	0.008*
WOMAC Pain	5.8 ± 3.9	6.5 ± 2.8	0.542	7.6 ± 4.3	2.2 ± 3.4	< 0.001*	0.274	0.004*	0.414	0.005*	0.002*
WOMAC Stiffness	2.7 ± 2.7	2.5 ± 2.6	0.786	2.2 ± 1.7	1.4 ± 1.8	0.237	0.425	0.190	0.113	0.257	0.816
WOMAC Physical function	22.1 ± 10.3	22.5 ± 7.8	0.900	24.6 ± 13.9	8.3 ± 12.5	< 0.001*	0.760	0.003*	0.224	0.003*	0.005*
WOMAC TOTAL	31.5 ± 15.8	33.2 ± 11.7	0.749	35.3 ± 19.2	12.4 ± 18.2	< 0.001*	0.680	0.003*	0.193	0.003*	0.005*

SD standard deviation, *VAS* visual analog scale, *KOOS-PS* knee injury and osteoarthritis outcome score physical function short form, *OKS* Oxford knee score, *TSK* Tampa scale for kinesiophobia, *SF-12* short-form health survey, *PCS* physical, *MCS* mental, *LEFS* lower extremity functional scale, *WOMAC* Western Ontario and McMaster Universities Osteoarthritis index

* $p < 0.05$

Table 5 Intragroup and intergroup evaluation of prone and supine proprioception scores

			Meniscopathy			Contralateral					Interaction		
			Pre	Post		Pre	Post		Pre vs. Pre	Post vs. Post	Group	Time	Group x Time
			Mean ± SD	*Mean ± SD*	*P*	*Mean ± SD*	*Mean ± SD*	*P*	*P*	*P*	*P*	*P*	*P*
Collagen	Face down	15°	4.7 ± 2.6	4 ± 3	0.555	5.8 ± 3.7	3 ± 4.9	0.024*	0.337	0.468	0.976	0.044*	0.218
		30°	4.8 ± 3.7	5.7 ± 4.9	0.410	7.2 ± 4.3	4.7 ± 3.5	0.044*	0.090	0.505	0.544	0.380	0.046*
		45°	5.4 ± 4.1	7.2 ± 7.1	0.139	6.2 ± 4.2	4.5 ± 3.4	0.184	0.540	0.170	0.536	0.911	0.051
		60°	6.8 ± 4.5	6.4 ± 5	0.792	5.5 ± 3.8	4 ± 2.4	0.270	0.355	0.079	0.073	0.334	0.549
	Supine Position	15°	5.4 ± 3.6	4.8 ± 3.9	0.539	3.3 ± 2.5	6.3 ± 4	0.007*	0.049*	0.258	0.742	0.124	0.020*
		30°	3.9 ± 3.7	2.3 ± 2	0.246	11.8 ± 4.9	4.5 ± 4.1	< 0.001*	< 0.001*	0.049*	< 0.001*	< 0.001*	0.008*
		45°	4 ± 3.2	3.4 ± 2.3	0.586	5.7 ± 3.4	4.6 ± 3.3	0.361	0.148	0.208	0.040*	0.304	0.791
		60°	4.9 ± 4.2	3.2 ± 2.2	0.173	5.9 ± 3.8	6.6 ± 3.7	0.611	0.463	0.003*	0.016*	0.538	0.187
Placebo	Face down	15°	4.5 ± 2.9	4.9 ± 3.8	0.823	4.7 ± 4.4	6.7 ± 4.4	0.244	0.872	0.227	0.206	0.325	0.500
		30°	4.7 ± 3.4	6.3 ± 6.3	0.306	3.7 ± 2.8	3.3 ± 3.1	0.791	0.356	0.109	0.072	0.588	0.362
		45°	4.5 ± 2.7	4.8 ± 3.2	0.714	5.4 ± 2.3	5.6 ± 3.8	0.845	0.331	0.574	0.346	0.691	0.903
		60°	4.7 ± 4.1	5.6 ± 4.3	0.619	4.8 ± 2.7	7.6 ± 5.5	0.101	0.960	0.264	0.307	0.131	0.406
	Supine Position	15°	4.5 ± 2.9	3 ± 3.6	0.166	3.7 ± 3.4	4.9 ± 2.4	0.285	0.472	0.107	0.550	0.817	0.087
		30°	3.5 ± 2.9	4.6 ± 2.5	0.339	13.6 ± 4.9	4 ± 3.7	< 0.001*	< 0.001*	0.608	< 0.001*	< 0.001*	< 0.001*
		45°	4 ± 4.1	3.5 ± 3.2	0.637	4.6 ± 2.4	3 ± 2.1	0.157	0.656	0.592	0.990	0.183	0.495
		60°	5.3 ± 3.5	5.3 ± 4.6	0.974	5.4 ± 3.8	3.3 ± 2.7	0.128	0.907	0.145	0.313	0.287	0.267

* $p < 0.05$

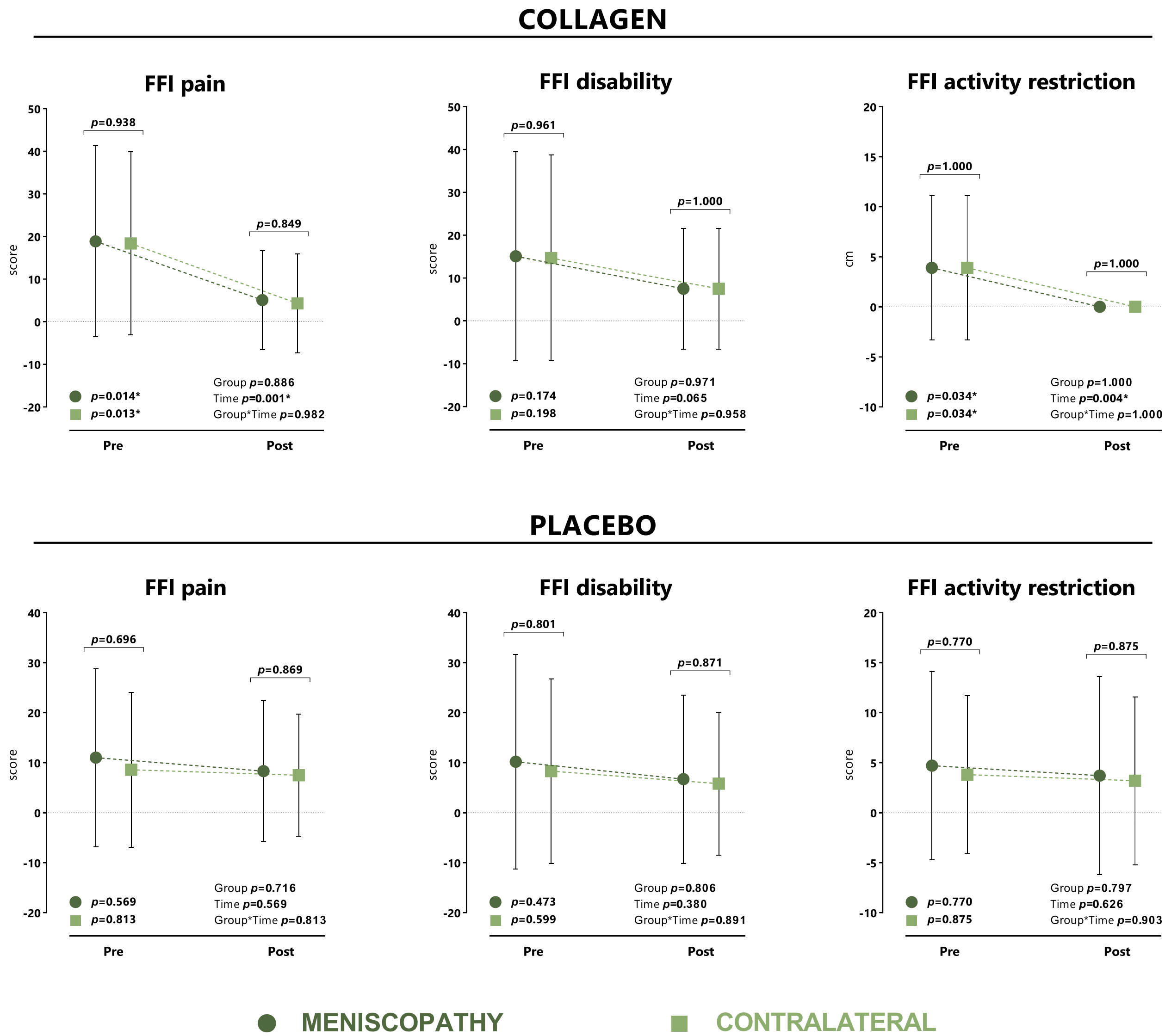

Fig. 2 Intragroup and intergroup evaluation of foot function index results. *$p < 0.05$; FFI foot function index

staging system developed by Fischer et al. [9]. The main finding of the study showed that eight weeks of supplementation with various collagen types had statistically significant effects on pain, quality of life, kinesiophobia, and foot function scale scores in patients with meniscopathy. Similarly, eight weeks of supplementation showed a near statistically significant difference in leg strength ($p = 0.057$), but no significant difference was found in back strength, proprioception, balance, and various functional test results.

Meniscopathy is a common disease that significantly affects the functional and biomechanical structure of the knee [39]. The meniscus plays an important role in load transmission, joint lubrication, stability, shock absorption, and proprioception [40–42]. Therefore, various conservative and surgical treatment methods are utilized after meniscopathy, depending on the degree of tear [43–45]. However, researchers have recently focused on alternative treatment methods in order to preserve the meniscus function fully [7, 13–15]. As an alternative method, oral administration of type I collagen, which is the main component of the meniscus, is thought to be beneficial on the negative effects of meniscopathy [46].

The evaluation of various factors such as pain, kinesiophobia, and functional status that commonly occur after meniscopathy is very important in terms of understanding both the level of disease and the effects of the treatment method. In the WOMAC pain and VAS

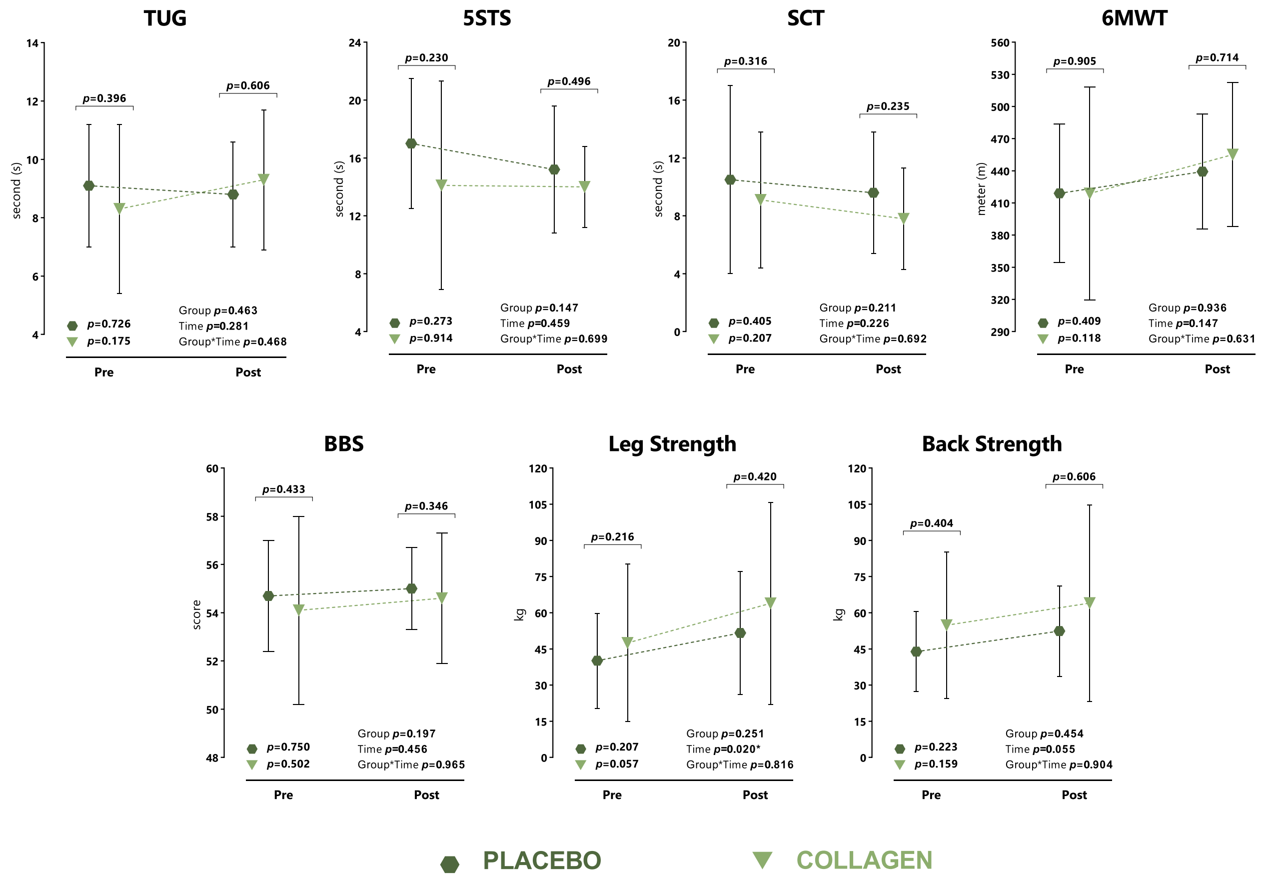

Fig. 3 Intragroup and intergroup evaluation of functional test and scale results. *$p < 0.05$; TUG timed up and go Test; 5STS the five repetitions sit to stand Test; SCT stair-climbing Test; 6MWT six-minute walking test BBS berg balance scale

scores included in our study, eight weeks of collagen supplementation had a significant positive effect on the pain level. This result was similar to previous studies evaluating the effects of collagen supplementation on different knee injuries, especially osteoarthritis [30, 47–51]. Uncontrolled damage to mechanoreceptors occurs after meniscopathy [52]. This damage causes irregular afferent impulses in healthy mechanoreceptors, leading to decreased proprioceptive sensation [53]. When this decrease in proprioceptive sensation is combined with other biomechanical effects that occur after injury in the knee joint, it may have an effect on kinesiophobia, quality of life, functional capacity, and strength levels in addition to pain. Similar to the pain scale scores, eight-week collagen supplementation in our study also had positive effects on quality-of-life scores such as WOMAC, KOOS-PS, OKS, SF-12, LEFS, FFI, and kinesiophobia scores evaluated with TSK. Although studies evaluating collagen supplementation in patients with meniscopathy are very limited in the literature, researchers have reported similar positive effects in various studies evaluating the quality of life and kinesiophobia levels in different knee injuries [51, 54]. Collagen produces anti-inflammatory cytokines that stimulate chondrocytes and are responsible for the synthesis of cartilage matrix components by induction and migration of regulatory T cells to the site of inflammation and damage [55]. Therefore, the positive effects of collagen supplementation on pain, quality of life, and kinesiophobia levels in our study can be explained by the protective effect of collagen on cartilage.

Since various parts of the meniscus are innervated by mechanoreceptors that provide proprioceptive and sensory function, proprioceptive sensory loss may occur in the knee joint after meniscal injury [56]. In the proprioceptive sensory evaluation performed in our study, it was found that eight weeks of collagen supplementation contributed to significant improvements on the contralateral side, although it showed similar results on the side with meniscal injury. These variable effects of collagen supplementation may depend on the severity of the meniscal tear, the individual differences of the patients, and the level of functional differences with the healthy knee.

Mechanoreceptor injury due to meniscal tears may be associated with decreased proprioception as well as postural stability and balance [52]. Taşkın et al. (2022) [57] found that the use of collagen supplementation for 12 weeks positively affected balance performances in their study with male patients with meniscopathy. In our study, BBS was used to assess the level of balance and the results showed that there was no statistical difference after collagen supplementation. For the BBS, scores above 41 are considered a low fall risk [58]. The BBS scores in the study show that even before supplementation, both subject groups had a low fall risk (placebo = 54.7 ± 2.3 and collagen = 54.1 ± 3.9). Therefore, the low fall risk of the subjects before supplementation may have played an important role in the lack of significant differences between pre- and post-tests.

After meniscopathy, patients are likely to experience a significant deficit in functional capacity due to negative effects on pain and proprioceptive sensation. After eight weeks of collagen supplementation, no difference was observed in TUG, 6MWT, 5STS, and SCT tests in which functional capacities were evaluated. Similarly, no difference was observed in the back strength assessment included in the study. However, collagen supplementation was significantly effective on leg strength, although not statistically significant ($p = 0.057$). Musculoskeletal pain perception and kinesiophobia limit the performance of repetitive activities, reduce range of motion, and lead to a decrease in physical capacity by reducing power production [5]. Collagen utilization promotes bone strength, density, and joint stability [57]. Although it was observed that collagen usage made positive contributions especially in terms of physiological characteristics such as pain [27–30, 47, 51], these effects were observed to be more limited in functional performance evaluations [57]. Therefore, improvements in pain and kinesiophobia levels due to collagen use and the effects of collagen on bone structure may have played a role in the increase in leg strength.

In addition to collagen, the supplement used in our study also contained ingredients such as hyaluronic acid, glucosamine sulfate, and chondroitin sulfate, which have proven to be effective in the treatment of pain related to knee joint injuries [59, 60]. Therefore, in addition to collagen, other effective ingredients in the product may have played a role in the positive effects of eight weeks of supplementation on pain and quality of life. However, a clearer understanding of this depends on comparing the ingredients in separate groups.

This study had several limitations, including the groups having the minimum number of subjects allowed by power analysis, the relatively wide age range of all participants, differences in the types and levels of meniscal injury, not differentiating between internal and external meniscus in injury evaluations, lack of gender-specific assessments, duration of supplement use, and evaluation of a single product with varying amounts of ingredients. Nevertheless, our study showed that eight weeks of collagen supplementation significantly improved pain, kinesiophobia, quality of life, and leg strength levels in patients with meniscopathy. However, similar results were seen in other functional tests. Although there are studies examining the effects of collagen supplementation in the treatment of various knee injuries [29, 30, 47, 49, 51, 54, 61], studies specifically evaluating the effects of collagen supplementation in meniscus injuries are very limited [27, 57]. Therefore, supportive studies similar to our study are needed to associate the effects of collagen supplementation with meniscal tissue directly. In addition, in future studies, separate evaluations of collagen supplementation in different groups in terms of age, gender, and meniscopathy levels may allow a clearer understanding of the treatment effects. Considering that another important factor is the duration of supplement use, longer supplement use and regular follow-up in future studies may contribute to revealing the effects of collagen in more detail.

Conclusions

Our study showed that eight weeks of collagen supplementation significantly improved pain, kinesiophobia, quality of life and leg strength levels in patients with meniscopathy. However, other functional tests showed similar results between groups. Although positive effects of collagen supplementation were observed in patients with meniscopathy, additional studies with different designs are needed to better understand the effects of this supplementation.

Abbreviations

5STS	The Five Repetition Sit to Stand Test
6MWT	6-Minute Walking Test
BBS	Berg Balance Scale
BMI	Body Mass Index
FFI	Foot Function Index
KOOS-PS	Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form
LEFS	Lower Extremity Functional Scale
MCS	Mental Component Score
OKS	Oxford Knee Score
PCS	Physical Component Score
RM ANOVA	Repeated-measures Analysis of Variance
SCT	Stair-Climbing Test
SD	Standard Deviation
SF-12	Short Form Health Survey
TSK	Tampa Scale for Kinesiophobia
TUG	Timed Up and Go
VAS	Visual Analog Scale
WOMAC	Western Ontario and McMaster Universities Osteoarthrtis Index

Acknowledgements

Not applicable.

Authors' contributions
The first draft of the manuscript and the revised manuscript were written by ASG, AKY, BA, EKS, EA, BG and AM, and HAY, NG and LK completed the data analysis and suggested revisions to the manuscript. HAY and LK participated in the design of the study and performed the statistical analysis, AKY and BG conceived of the study and participated in its design and coordination and helped to draft the manuscript. BA, EKS and EA completed the visualization. All authors read and approved the final manuscript.

Funding
This research received no external funding.

Data availability
Data supporting the findings of this study are available through the corresponding author, but restrictions apply to the availability of these data used for the current study and are therefore not publicly available. However, data are available from the corresponding author (akerim.yilmaz@omu.edu.tr) upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in compliance with the ethical principles stated in the Declaration of Helsinki and ICH Good Clinical Practice guidelines. Ethics committee approval was obtained from Sinop University Human Research Ethics Committee (protocol no: 2023/182) and registered in the Iranian Clinical Trials Registry on 14/05/2024 with the number IRCT20240411061470N2. Participants were included in the study after written informed consent forms were collected.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Orthopedics and Traumatology, Samsun Education and Research Hospital, Samsun 55090, Turkey. [2]Faculty of Yaşar Doğu Sport Sciences, Ondokuz Mayıs University, Samsun 55270, Turkey. [3]Department of Internal Medicine, Samsun Alaçam State Hospital, Samsun 55800, Turkey. [4]Department of Physical Education and Sports, Faculty of Sports Sciences, Sinop University, Sinop 57010, Turkey. [5]Department of Orthopedic Physiotherapy, Faculty of Physical Therapy and Rehabilitation, Dokuz Eylül University, İzmir 35340, Turkey. [6]Department of Orthopaedics and Traumatology, Faculty of Medicine, Dokuz Eylül University, İzmir 35340, Turkey.

Received: 6 June 2024 Accepted: 23 December 2024
Published online: 04 January 2025

References
1. Belk JW, Kraeutler MJ, Thon SG, Littlefield CP, Smith JH, McCarty EC. Augmentation of Meniscal Repair With Platelet-Rich Plasma: A Systematic Review of Comparative Studies. Orthop J Sport Med. 2020;8:232596712092614. https://doi.org/10.1177/2325967120926145.
2. Bryceland JK, Powell AJ, Nunn T. Knee Menisci. Cartilage. 2017;8:99–104. https://doi.org/10.1177/1947603516654945.
3. Berton A, Longo UG, Candela V, Greco F, Martina FM, Quattrocchi CC, et al. Quantitative Evaluation of Meniscal Healing Process of Degenerative Meniscus Lesions Treated with Hyaluronic Acid: A Clinical and MRI Study. J Clin Med. 2020;9:2280. https://doi.org/10.3390/jcm9072280.
4. Khetia EA, McKeon BP. Meniscal Allografts: Biomechanics and Techniques. Sports Med Arthrosc. 2007;15:114–20. https://doi.org/10.1097/JSA.0b013e3180dca217.
5. Gevrek C, Atay AÖ, Kınıklı Gİ. Evaluation of Force Sense, Functional Performance, Quality of Life, Activity Level and Kinesiophobia in Degenerative Meniscal Tears Following Partial Meniscectomy. J Basic Clin Heal Sci. 2023;7:426–35. https://doi.org/10.30621/jbachs.1155794.
6. Chirichella PS, Jow S, Iacono S, Wey HE, Malanga GA. Treatment of Knee Meniscus Pathology: Rehabilitation, Surgery, and Orthobiologics. PM&R. 2019;11:292–308. https://doi.org/10.1016/j.pmrj.2018.08.384.
7. Dangelmajer S, Familiari F, Simonetta R, Kaymakoglu M, Huri G. Meniscal Transplants and Scaffolds: A Systematic Review of the Literature. Knee Surg Relat Res. 2017;29:3–10. https://doi.org/10.5792/ksrr.16.059.
8. Wells ME, Scanaliato JP, Dunn JC, Garcia EJ. Meniscal Injuries: Mechanism and Classification. Sports Med Arthrosc. 2021;29:154–7. https://doi.org/10.1097/JSA.0000000000000311.
9. Fischer SP, Fox JM, Del Pizzo W, Friedman MJ, Snyder SJ, Ferkel RD. Accuracy of diagnoses from magnetic resonance imaging of the knee. A multi-center analysis of one thousand and fourteen patients. J Bone Jt Surg. 1991;73:2–10.
10. Bansal S, Floyd ER, Kowalski MA, Aikman E, Elrod P, Burkey K, et al. Meniscal repair: The current state and recent advances in augmentation. J Orthop Res. 2021;39:1368–82. https://doi.org/10.1002/jor.25021.
11. Bhatia S, LaPrade CM, Ellman MB, LaPrade RF. Meniscal Root Tears. Am J Sports Med. 2014;42:3016–30. https://doi.org/10.1177/0363546514524162.
12. Hutchinson ID, Moran CJ, Potter HG, Warren RF, Rodeo SA. Restoration of the Meniscus. Am J Sports Med. 2014;42:987–98. https://doi.org/10.1177/0363546513498503.
13. Venkataraman S, Ethiraj P, Shanthappa AH, Vellingiri K. Association of Meniscus Injuries in Patients With Anterior Cruciate Ligament Injuries. Cureus. 2022;14:e25878. https://doi.org/10.7759/cureus.25878.
14. DeFroda SF, Yang DS, Donnelly JC, Bokshan SL, Owens BD, Daniels AH. Trends in the surgical treatment of meniscal tears in patients with and without concurrent anterior cruciate ligament tears. Phys Sportsmed. 2020;48:229–35. https://doi.org/10.1080/00913847.2019.1685363.
15. Parker BR, Hurwitz S, Spang J, Creighton R, Kamath G. Surgical Trends in the Treatment of Meniscal Tears. Am J Sports Med. 2016;44:1717–23. https://doi.org/10.1177/0363546516638082.
16. Yim J-H, Seon J-K, Song E-K, Choi J-I, Kim M-C, Lee K-B, et al. A Comparative Study of Meniscectomy and Nonoperative Treatment for Degenerative Horizontal Tears of the Medial Meniscus. Am J Sports Med. 2013;41:1565–70. https://doi.org/10.1177/0363546513488518.
17. Herrlin SV, Wange PO, Lapidus G, Hållander M, Werner S, Weidenhielm L. Is arthroscopic surgery beneficial in treating non-traumatic, degenerative medial meniscal tears? A five year follow-up. Knee Surgery, Sport Traumatol Arthrosc. 2013;21:358–64. https://doi.org/10.1007/s00167-012-1960-3.
18. Nezu M, Kudo M, Morimoto R, Ono Y, Omata K, Tezuka Y, et al. Effects of surgical treatment for acromegaly on knee MRI structural features. Endocr J. 2018;65:991–9. https://doi.org/10.1507/endocrj.EJ18-0108.
19. Rajani AM, Shah UA, Mittal A, Gupta S, Garg R, Rajani AA, et al. AMR Sign - An Arthroscopic S-shaped Fold Signifying Adequate Medial Meniscus Repair. Malaysian Orthop J. 2023;17:13–20. https://doi.org/10.5704/MOJ.2307.003.
20. Makris EA, Hadidi P, Athanasiou KA. The knee meniscus: Structure–function, pathophysiology, current repair techniques, and prospects for regeneration. Biomaterials. 2011;32:7411–31. https://doi.org/10.1016/j.biomaterials.2011.06.037.
21. Chevrier A, Nelea M, Hurtig MB, Hoemann CD, Buschmann MD. Meniscus structure in human, sheep, and rabbit for animal models of meniscus repair. J Orthop Res. 2009;27:1197–203. https://doi.org/10.1002/jor.20869.
22. Andrews SHJ, Rattner JB, Abusara Z, Adesida A, Shrive NG, Ronsky JL. Tie-fibre structure and organization in the knee menisci. J Anat. 2014;224:531–7. https://doi.org/10.1111/joa.12170.
23. Baker BM, Shah RP, Huang AH, Mauck RL. Dynamic Tensile Loading Improves the Functional Properties of Mesenchymal Stem Cell-Laden Nanofiber-Based Fibrocartilage. Tissue Eng Part A. 2011;17:1445–55. https://doi.org/10.1089/ten.tea.2010.0535.
24. Katz JN. Editorial: Prevalence of Arthritis Revisited. Arthritis Rheumatol. 2018;70:153–4. https://doi.org/10.1002/art.40357.
25. Gao S-G, Zeng C, Liu J-J, Tian J, Cheng C, Zhang F-J, et al. Association between Wnt inhibitory factor-1 expression levels in articular cartilage and the disease severity of patients with osteoarthritis of the knee. Exp Ther Med. 2016;11:1405–9. https://doi.org/10.3892/etm.2016.3049.
26. Zdzieblik D, Oesser S, Gollhofer A, König D. Improvement of activity-related knee joint discomfort following supplementation of specific collagen peptides. Appl Physiol Nutr Metab. 2017;42:588–95. https://doi.org/10.1139/apnm-2016-0390.

27. Bello AE, Oesser S. Collagen hydrolysate for the treatment of osteoarthritis and other joint disorders: a review of the literature. Curr Med Res Opin. 2006;22:2221–32. https://doi.org/10.1185/030079906X148373.
28. Benito-Ruiz P, Camacho-Zambrano MMM, Carrillo-Arcentales JNN, Mestanza-Peralta MAA, Vallejo-Flores CAA, Vargas-López SVV, et al. A randomized controlled trial on the efficacy and safety of a food ingredient, collagen hydrolysate, for improving joint comfort. Int J Food Sci Nutr. 2009;60(Suppl 2):99–113. https://doi.org/10.1080/09637480802498820.
29. Moskowitz RW. Role of collagen hydrolysate in bone and joint disease. Semin Arthritis Rheum. 2000;30:87–99. https://doi.org/10.1053/sarh.2000.9622.
30. Luo C, Su W, Song Y, Srivastava S. Efficacy and safety of native type II collagen in modulating knee osteoarthritis symptoms: a randomised, double-blind, placebo-controlled trial. J Exp Orthop. 2022;9:123. https://doi.org/10.1186/s40634-022-00559-8.
31. Alghadir A, Anwer S, Iqbal A, Iqbal Z. Test–retest reliability, validity, and minimum detectable change of visual analog, numerical rating, and verbal rating scales for measurement of osteoarthritic knee pain. J Pain Res. 2018;11:851–6. https://doi.org/10.2147/JPR.S158847.
32. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol. 1988;15:1833–40.
33. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)—Development of a Self-Administered Outcome Measure. J Orthop Sport Phys Ther. 1998;28:88–96. https://doi.org/10.2519/jospt.1998.28.2.88.
34. Harris K, Dawson J, Doll H, Field RE, Murray DW, Fitzpatrick R, et al. Can pain and function be distinguished in the Oxford Knee Score in a meaningful way? An exploratory and confirmatory factor analysis. Qual Life Res. 2013;22:2561–8. https://doi.org/10.1007/s11136-013-0393-x.
35. Miller RP, Kori SH, Todd DD. The Tampa Scale: a measure of kinisophobia. Clin J Pain. 1991;7:51.
36. Ware JE, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey. Med Care. 1996;34:220–33. https://doi.org/10.1097/00005650-199603000-00003.
37. Binkley JM, Stratford PW, Lott SA, Riddle DL. The Lower Extremity Functional Scale (LEFS): Scale Development, Measurement Properties, and Clinical Application. Phys Ther. 1999;79:371–83. https://doi.org/10.1093/ptj/79.4.371.
38. Budiman-Mak E, Conrad KJ, Roach KE. The foot function index: A measure of foot pain and disability. J Clin Epidemiol. 1991;44:561–70. https://doi.org/10.1016/0895-4356(91)90220-4.
39. Hung TNK, Vy VPT, Tri NM, Hoang LN, Van TL, Ho QT, et al. Automatic Detection of Meniscus Tears Using Backbone Convolutional Neural Networks on Knee MRI. J Magn Reson imaging. 2023;57:740–9. https://doi.org/10.1002/jmri.28284.
40. Fox AJS, Wanivenhaus F, Burge AJ, Warren RF, Rodeo SA. The human meniscus: A review of anatomy, function, injury, and advances in treatment. Clin Anat. 2015;28:269–87. https://doi.org/10.1002/ca.22456.
41. Adams BG, Houston MN, Cameron KL. The Epidemiology of Meniscus Injury. Sports Med Arthrosc. 2021;29:e24-33. https://doi.org/10.1097/JSA.0000000000000329.
42. Kang D-G, Park Y-J, Yu J-H, Oh J-B, Lee D-Y. A Systematic Review and Meta-Analysis of Arthroscopic Meniscus Repair in Young Patients: Comparison of All-Inside and Inside-Out Suture Techniques. Knee Surg Relat Res. 2019;31:1–11. https://doi.org/10.5792/ksrr.17.078.
43. Lavender C, Flores K, Patel T, Berdis G, Blickenstaff B. Nanoscopic Medial Meniscus Repair Arthrosc Tech. 2021;10:e1943–7. https://doi.org/10.1016/j.eats.2021.04.024.
44. Agrawal AK. Mulberry Knot Technique for Arthroscopic Meniscus Repair. J Skelet Syst. 2022;1:01–3. https://doi.org/10.58489/2836-2284/004.
45. van Well EB, Wijn SRW, Hannink G, Grutters JPC, Rovers MM. The value of reducing arthroscopic partial meniscectomy in the treatment of degenerative meniscus tears: a budget impact analysis. Int J Technol Assess Health Care. 2023;39: e7. https://doi.org/10.1017/S0266462322003361.
46. Ciemniewska-Gorzela K, Górecki J, Wojtkowiak D, Henklewski R, Żak-Pałczynska K, Murray J, et al. Biomechanical Comparison of the Simple Suture Technique, Meniscal Matrix-Assisted Repair, and a Novel Meniscus Cap Suture Technique for Complex Meniscal Repair. Orthop J Sport Med. 2023;11:23259671231217440. https://doi.org/10.1177/23259671231217439.
47. Chen C-C, Chang S-S, Chang C-H, Hu C-C, Nakao Y, Yong SM, et al. Randomized, double-blind, four-arm pilot study on the effects of chicken essence and type II collagen hydrolysate on joint, bone, and muscle functions. Nutr J. 2023;22:17. https://doi.org/10.1186/s12937-023-00837-w.
48. Kamat YD, Das B, Thakkar K, Mahajan M. A Retrospective Observational Study Evaluating the Synergistic Effect of a Novel Combination of Alfapin + Native Type 2 Collagen + Mobilee (Hyaluronic Acid) + CurQlife (Curcumin) Nutraceuticals in the Symptomatic Improvement of Knee Osteoarthritis. Cureus. 2023;15:e36123. https://doi.org/10.7759/cureus.36123.
49. Kumar P, Bansal P, Rajnish RK, Sharma S, Dhillon MS, Patel S, et al. Efficacy of undenatured collagen in knee osteoarthritis: review of the literature with limited meta-analysis. Am J Transl Res. 2023;15:5545–55.
50. He Z, Li S, Zou J, Gong Z, He L, Zhang Z, et al. Pain-Related Risk Factors Among Radiologic Stages of Knee Osteoarthritis: Data From the Osteoarthritis Initiative. Arthritis Care Res (Hoboken). 2023;75:1333–9. https://doi.org/10.1002/acr.24997.
51. Santana ÉTN, da Cunha MS, Brandão Lima VN, DeSantana Filho VJ, dos Santos Maciel LY, de Farias Neto JP, et al. Comparison between exercise therapy and non-hydrolyzed collagen (UC-II) in functionality and quality of life in women with knee osteoarthritis. Wien Klin Wochenschr. 2023;135:291–300. https://doi.org/10.1007/s00508-022-02037-8.
52. Lee J-H, Heo J-W, Lee D-H. Comparative postural stability in patients with lateral meniscus versus medial meniscus tears. Knee. 2018;25:256–61. https://doi.org/10.1016/j.knee.2018.01.012.
53. Wang B, Zhong J-L, Xu X-H, Shang J, Lin N, Lu H-D. Incidence and risk factors of joint stiffness after Anterior Cruciate Ligament reconstruction. J Orthop Surg Res. 2020;15:175. https://doi.org/10.1186/s13018-020-01694-7.
54. Bongers CCWG, Ten Haaf DSM, Catoire M, Kersten B, Wouters JA, Eijsvogels TMH, et al. Effectiveness of collagen supplementation on pain scores in healthy individuals with self-reported knee pain: a randomized controlled trial. Appl Physiol Nutr Metab. 2020;45:793–800. https://doi.org/10.1139/apnm-2019-0654.
55. van Meegeren MER, Roosendaal G, Jansen NWD, Wenting MJG, van Wesel ACW, van Roon JAG, et al. IL-4 alone and in combination with IL-10 protects against blood-induced cartilage damage. Osteoarthr Cartil. 2012;20:764–72. https://doi.org/10.1016/j.joca.2012.04.002.
56. Lee D-H, Lee J-H, Ahn S-E, Park M-J. Effect of Time after Anterior Cruciate Ligament Tears on Proprioception and Postural Stability. PLoS One. 2015;10:e0139038. https://doi.org/10.1371/journal.pone.0139038.
57. Taşkın C, Taşkın AK, Yılmaz M, Delıhacıoğlu CC, Tümkaya Ü, Yamakoğlu E. The Effect of Type-II Collagen on Y-Balance Performance in Men With Meniscus. Prog Nutr. 2022;24:e2022012. https://doi.org/10.23751/pn.v24i1.11648.
58. Ray GM, Dhote PR, Rupani A. Effect of 5-week training session on balance in elderly with medium risk of fall: a comparative study. Int J Sci Reports. 2023;9:183–91. https://doi.org/10.18203/issn.2454-2156.IntJSciRep20231447.
59. Lomonte ABV, Mendonça JA, de Castro BG, Castro ML. Multicenter, randomized, double-blind clinical trial to evaluate efficacy and safety of combined glucosamine sulfate and chondroitin sulfate capsules for treating knee osteoarthritis. Adv Rheumatol. 2018;58:41. https://doi.org/10.1186/s42358-018-0041-9.
60. Nelson FR, Zvirbulis RA, Zonca B, Li KW, Turner SM, Pasierb M, et al. The effects of an oral preparation containing hyaluronic acid (Oralvisc®) on obese knee osteoarthritis patients determined by pain, function, bradykinin, leptin, inflammatory cytokines, and heavy water analyses. Rheumatol Int. 2015;35:43–52. https://doi.org/10.1007/s00296-014-3047-6.
61. Genç AS, Yılmaz AK, Anıl B, Korkmaz Salkılıç E, Akdemir E, Sancaklı A, et al. Effect of supplementation with type 1 and type 3 collagen peptide and type 2 hydrolyzed collagen on osteoarthritis-related pain, quality of life, and physical function: A double-blind, randomized, placebo-controlled study. Jt Dis Relat Surg. 2024. https://doi.org/10.52312/jdrs.2025.1965.

Publisher's Note