

## İs Combined Acellular Collagen Matrix and High Tibial Osteotomy Treatment Effective In Osteochondral Defects? Preliminary Study

Kombine Asellular Kollajen Matrisi ve Yüksek Tibial Osteotomi Tedavisi Osteokondral Kusurlarda Etkili Midir? Ön çalışma

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### ABSTRACT

**Aim:** In this study, we want to compare clinical and radiological results of 12 patient treated with acellular collagen matrix (ACM) and High Tibial osteotomy-cellular collagen matrix(ACM-HTO) combination.

**Method:** In this study, we evaluated 12 patients with chondral lesion prospectively the years of between 2014- 2016 after ethical approval. Cartilage damage was diagnosed with MRI and cartilage degeneration volume was calculated with Mimics medical image processing software and axis deviation was diagnosed with ortho X-ray. Patients were divided into two groups. ACM only (Group 1) and ACM- HTO (Group 2).

**Results:** ACM only group consists of 5 patients. Preoperative mean of chondral lesion volume was  $77.11 \pm 137.5$  (0.27-321.61). Post-operative mean Knee score was  $175.20 \pm 24.4$  (150-203) and chondral lesion volume was  $0.3 \pm 0.03$  (0-0.8). ACM-HTO group consists of 7 patients. Preoperative mean of chondral lesion volume was  $112.72 \pm 239$  (0.27- 653). Post-operative mean of HSS score was  $155 \pm 20.4$  (135-183) and chondral lesion volume was  $0.26 \pm 0.09$  (0-0.69).

**Conclusion:** According to these results, all patients' HSS scores and Cartilage volume are increased, but there were no significant differences were found between two groups.

Keywords: cartilage, high tibial osteotomy, acellular collagen matrix

### ÖZET

**Amaç:** Bu çalışmada, asellüler kollajen matrisi (AKM) ve Yüksek Tibial osteotomi-hücreli kollajen matrisi (AKM-YTO) kombinasyonu ile tedavi edilen 12 hastanın klinik ve radyolojik sonuçlarını karşılaştırmak istedik.

**Yöntem:** Bu çalışmada, 2014-2016 yılları arasında etik onayları alındıktan sonra kondral lezyonu olan 12 hasta prospektif olarak değerlendirildi. Manyetik rezonans görüntüleme(MRG) ile kırıkda hasarı tespit edildi ve kırıkda dejenerasyonun hacmi Mimics medikal görüntü işleme yazılım sistemi ile hesaplandı ve eksen sapması ise X-ray ile teşhis edildi. Hastalar sadece AKM(Grup 1) ve kombine AKM-YTO(Grup 2) olmak üzere iki gruba ayrıldı.

**Bulgular:** Sadece AKM grubu 5 hastadan oluşmaktadır. Bu grupta ameliyat öncesi ortalama kırıkda lezyon hacmi  $77.11 \pm 137.5$  (0.27- 321.61) idi. Operasyon sonrası ortalama diz(HSS) skoru  $175.20 \pm 24.4$  (150-203) ve kırıkda lezyon hacmi  $0.3 \pm 0.03$  (0-0.8) idi. AKM-YTO grubu 7 hastadan oluşmaktadır. Bu grupta ise ameliyat öncesi ortalama kırıkda lezyon hacmi  $112.72 \pm 239$  (0.27-653) idi. Ameliyat sonrası ortalama diz(HSS) skoru  $155 \pm 20.4$  (135-183) ve kırıkda lezyon hacmi  $0.26 \pm 0.09$  (0-0.69) idi.

**Sonuç:** Bu sonuçlara göre, tüm hastaların HSS skorları ve kırıkda hacmi artmıştır ancak iki grup arasında anlamlı bir farklılık bulunmamaktadır.

Anahtar Kelimeler: Kırıkda, Yüksek Tibial Osteotomi, Asellüler Kollajen Matrisi

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Articular cartilage damage is unable to heal spontaneously and standard gold treatment modalities haven't been found yet. Besides many treatment modalities have been shown in the literature there is still lack of an effective treatment in medical area. Those treatments vary by the size and the duration of the lesion. The course of treatment from palliative to restorative phase consists of joint debridement and irrigation [1], viscosupplementation [2], microfracture [3], autologous chondrocyte implantation and osteochondral grafting. On the other hand, the replacement tissues are fibrous type cartilage and the technique, which is unable to be used on less than 4 cm defects and moreover postoperative 6-8 week of obligatory non-weight bearing ambulation are negatives of this technique. Osteochondral allografts are available for both arthroscopic and open surgeries [4]. Autologous chondrocyte implantation gives unlimited opportunity to seed various defect sizes and to produce hyaline cartilage at the end. In this method, a surgical intervention is needed to harvest cartilage cells to be used in the production of a cell culture and produced cells are transferred into defects in second surgery. The practice is expensive, invasive and requires waiting procedure for the cell growth and the application with few multiple surgeries. Also in order to keep the cells in the defect area, it is needed to create a periosteal flap to cover the cartilage surface and cultured cells are injected under the cover which is used widely [5-7]. If it is not possible to create cultured cartilage cells at the first hand, there are second and third generation autologous chondrocyte implantation techniques are described in the literature [8].

The aim in successive cartilage repair is to obtain a smooth surface on cartilage surface, ameliorate the symptoms of patients, restore the function, obtain a tissue most similar to normal hyaline cartilage biomechanically and biochemically and to prevent extension of cartilage defect to stop the development of arthrosis. High tibia osteotomies are well described and safe osteotomy procedure for treating unicompartmental arthrosis by changing mechanical axis of lower extremity. In this study, we want to compare clinical and radiological results of 12 patients treated with acellular collagen matrix (ACM) and High Tibial osteotomy-cellular collagen matrix (ACM-HTO) combination.

## MATERIAL-METHOD

In this study we evaluated 60 patients with chondral

lesion prospectively between 2014- 2016. Cartilage damage was diagnosed with 1.5 Tesla MRI (Siemens Magnetom; 1.5 T, Erlangen Germany) and cartilage degeneration volume was calculated with Mimics medical image processing software (Materialise NV Technologielaan Leuven Belgium) and axis deviation were diagnosed with ortho X-ray (General X-Ray System, 2006 Listern Tube Stand - Model SFC-31; Sandringham; England).

The inclusion criteria were single focal cartilage defect on medial or lateral compartment of the distal femur condyle, symptomatic lesions such as pain, swelling, locking and minimum 2 years clinical follow-up, patients treated with ACM with/without HTO. Patients age <18 and >60 years, rheumatological diseases, diffuse osteoarthritis, unstable knees, patients treated with only microfracture or only HTO were excluded. The radiological and clinical data of 12 patients were evaluated after receiving institutional review board. 20 patients treated with only arthroscopy, 12 treated with microfracture and 4 patients treated with only HTO were excluded. 12 Patients were divided into two groups. Only ACM and ACM-HTO. All the operations were performed by the same surgeons.

**Patients and treatment protocol:** Only ACM group consist of 5 patients. Mean age was  $50,60 \pm 11.05$  (35-60). 4 medial femoral condyle and 1 lateral femoral condyle were affected (Outerbridge grade III and IV). All patients were operated under spinal anesthesia and standard arthroscopic surgery procedure was applied. After determining chondral lesion, debridement was applied and subchondral bone plate was identified and mini arthrotomy was applied. Microfractures by 1.8 mm Kirschner wire nearly 3-4 mm apart and 5 mm in depth and ACM (Chondrofiller Gel; Amedix GmbH, Esslingen Germany) were applied after resolving at room temperature (25°C). Preoperatively mean chondral lesion volume was  $77.11 \pm 137.5$  (0.27- 321.61). Mean axis deviation  $-1.20 \pm 2.16$  (-4-1). Post operatively early active and passive range of motion exercises were started at the first day. Maximum knee flexion more than 90 degrees and full weight bearing (WB) didn't allowed until the end of one month. Partial WB was started at the end of one month and full WB was allowed after 2 months. ACM-HTO group consist of 7 patients. Mean age was  $49.71 \pm 8.9$  (34-58). All patients were operated under spinal anesthesia and standard arthroscopic surgery procedure was applied. All patients medial femoral condyle and additionally 2 pa-

tients patella posterior cartilage were affected(Outerbridge III and IV). After determining the chondral lesions mini arthroscopy and chondral debridement; microfracture and ACM (Figure 1) was applied like ACM group . Open wedge HTO(TST Tibbi Aletler San. Ve Tic. Ltd. Sti., İstanbul, Turkey) operation was performed and angulations were corrected by plate.

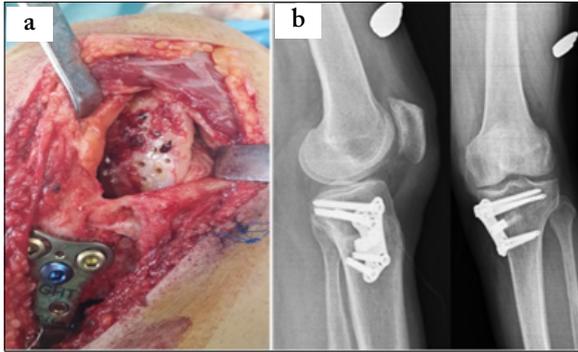


Figure 1: a) Intra operative view of HTO and medial chondral cartilage defect treated with ACM b) Post-operative X-Ray

**Fallow-up and eveluation:** All patients were followed at least two years. The mean follow up time was 26.4±4.3(24-36) Visual analog scale, Knee Scores [9] were recorded preoperatively, 6, 12, and 24 months postoperative. MRI evaluation(Figure 2) was performed after one and two year follow up and cartilage tissue volume was determined totally blinded by one orthopaedic surgeon and one anatomist. Cartilage tissue

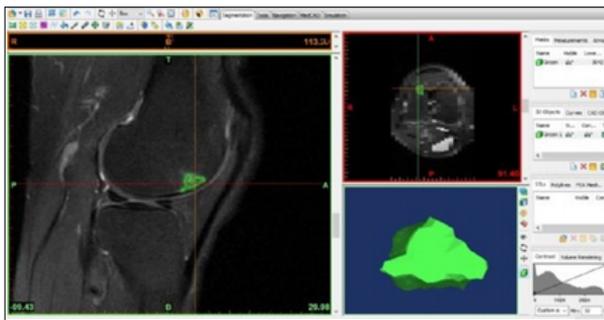


Figure 2: Pre-operative MRI view of a patient and chondral lesion measurement MFC: Medial Femoral Condyl, LFC: Lateral Femoral Condyl, PF: Patellofemoral

volume was calculated via MIMICS programme by one physiotherapist.

**Statistical analysis:** Statistical analysis were performed by SPSS 18 packet programme. Mann Whitney U test used for comparing datas pre and post-operatively. p<0.05 was set as level of significance.

**RESULTS**

Demographic datas of patients, Knee scores and chondral volumes pre- and postoperative were shown in Table 1 and 2. Post operatively early active and passive range of motion exercises were started at the first day. Maximum knee flexion more than 90 degrees and full weight bearing(WB) didn't allowed until the end of one month. Partial WB was started at the end of one month and full WB was allowed after 3 months.

Table 1: Pre-operative and post-operative measurement of chondral defects in patients

No	Age	Preop mm3	Postop mm3	Localisation	Additional operation	Preop Axis	Postop Axis
1	54	52,74	0	MFC	HTO	2(valgus)	12(valgus)
2	34	25,57	0	MFC	HTO	1(varus)	7(valgus)
3	50	54,74	0	MFC	HTO	2(varus)	5(valgus)
4	55	1,07	0,69	MFC + PF	HTO	1(varus)	6(valgus)
5	56	36,23	0,06	MFC	No	1(varus)	1(varus)
6	58	0,27	0	MFC	HTO	2(valgus)	6(valgus)
7	56	1,12	0	MFC + PF	HTO	4(valgus)	12(valgus)
8	60	321,64	0	MFC	No	2(valgus)	2(valgus)
9	59	1,57	0,01	MFC	No	1(varus)	1(varus)
10	43	0,27	0	MFC	Pin Fixation	4(valgus)	4(valgus)
11	41	653,55	0	MFC	HTO	6(varus)	2(valgus)
12	35	25,84	0,08	LFC	No	2(valgus)	2(valgus)

Table 2: Comparing groups according to Knee scores and radiographic changes

Group		Mean(±SD)	Min_Max.
1 (n=5)	Age	50,60(±11,06)	35_60
	Cartiagi defect Localisation	1,20(±0,45)	1_2
	Preop Cartilage Defect Volume	77,11(±137,57)	0,3_321,6
	Postop Cartilage Defect Volume	0,03(±0,04)	0_0,1
	Axis-Pre-op	-1,20(±2,17)	-4_1
	Axis Post-op	-1,20(±2,17)	-4_1
	Knee Score	175,20(±24,41)	150_203
2 (n=7)	Age	49,71(±8,92)	34_58
	Cartiagi defect Localisation	1,86(±1,46)	1_4
	Preop Cartilage defect	112,72(±239,66)	0,3_653,6
	Postop Cartilage Defect Volume	0,10(±0,26)	0_0,7
	Axis-Pre-op	0,29(±3,30)	-4_6
	Axis Post-op	-7,14(±3,67)	-12_-2
	Knee Score	155,0(±20,49)	135_183

In group 1 Preoperatively mean chondral lesion volume was 112.72±239 (0.27- 653). Mean axis deviation 0.29±3.3 (-4-6) degrees. Post-operatively mean HSS score was 175.20±24.4 (150-203), mean axis deviation-1.20±2.16(-4--1) and chondral lesion volume was 0.3±0.03(0-0.8) ( p<0.01). In group 2 Post-operatively mean HSS score was 155±20.4(135-183), mean axis deviation -7.14±3.67 (-12--2) and chondral lesion volume was 0.26±0.09 (0-0.69).

None of patient had total knee arthroplasty in two year period. One patient had hipertrophic scar tissue and flexion contracture in early follow up. Improvement after physical therapy was detected. One patient had second look arthroscopy procedure in Group 2 for

complex medial meniscus lesion and implant removal . We detected fullfilled cartilage was seen in this area (Figure 3)

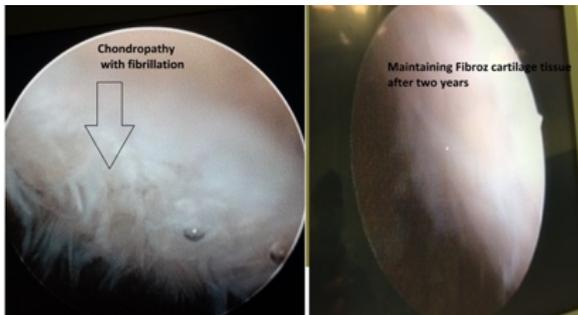


Figure 3: Perioperative view first and Second look arthroscopy view fibros cartilage tissues was maintained.

According to these results, all patients HSS scores and Cartilage volume were increased according to MRI results (Figure 4) but there were no significant differences were found into two groups( $p>0.05$ ).

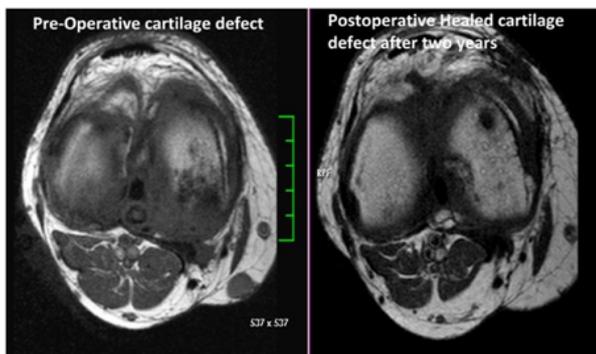


Figure 4: Pre and post operative cartilage defect

## DISCUSSION

Our study show that the application of ACM without HTO resulted better clinical outcomes. In group 1 Knee Score improvement was higher than group 2( $p<0.05$ ) but cartilage defect volume differences were nearly same in two group( $p>0.05$ ). It is not possible to find an ideal and standart technique that everybody settled on yet. It is needed to bring about new technologies and approaches to supply hyaline cartilage production in the defected and lesioned areas [10]. The main principle cartilage tissue engineering is to combine the convenient scaffold with preexisting lesion beneath intact cells. Some authors reported combination therapies about cartilage lesions. Clave et al reported Third-Generation Autologous Chondrocyte Implantation Versus Mosaicplasty for cartilage After

2 years, functional outcomes were significantly worse after treatment with Third-Generation Autologous Chondrocyte Implantation compared to mosaicplasty for isolated focal osteochondral defects of the femur [11]. Sofu et al reported also reported 2 different method for cartilage repair ; Hyaluronic Acid–Based Cell-Free Scaffold Application in Combination With Microfracture for the Treatment of Osteochondral Lesions of the Knee and clinical outcomes found better in Hyaluronic Acid–Based Cell-Free Scaffold [12].

High tibial osteotomy (HTO) is an accepted procedure to treat unicompartmental processes for mild osteoarthritis [13] by shifting the mechanical axis to realign the load. In our literature review we couldn't such a treatment modalities comparing Acellular Collagen Matrix with/out HTO.

Kahlenberg et al's study [14] about cartilage restoration techniques conjunction with HTO was microfracture. In this study, 839 knees were included in this study HTO had provides improvement functional status and delay to joint replacement surgery. In our clinic , we also use microfracture additional to HTO but in this study we only compare the patients whom are operated with acellular collagen matrix.

Some factors affect the functional results after HTO. Kumagai et al.[15] reported Body Mass Index(BMI), initial cartilage and postoperative limb alignment were major factors on HTO. Age, gender and clinical results were not affect the cartilage regeneration. We also found no statistically differences about age and gender. One of the major aim of this study is to evaluate the effect of axis correction on cartilage tissue repair. Tsukada et al.[16] compared moderate and overcorrected HTO on cartilage repair and had found no significant differences. In our study, we evaluated the effect of HTO on cartilage repair; in both group cartilage tissue coverage was maintained in MRI imaging but no significant differences found ( $p>0.01$ ).

**Limitations:** One of the limitation of this study is patient number. But our study is a prospective study and we include patients minimum two year follow up. Another limitation is cartilage volume measurement. We calculated cartilage lesions with MIMICS programme manually. Only one patient had second look arthroscopy so we couldn't had cartilage biopsies and know the type of repaired cartilage type.

**Conclusions:** Strenght of this study is a prospective

study and all operations were made by the same surgeon. Cartilage volume measured with a computational method.

Using Combined Acellular Collagen Matrix application with/out High Tibial Osteotomy treatment in local cartilage lesion of the knee was found effective, but there were no significant differences in both groups. Comparative improving techniques about cartilage repair should be made with further studies on more patients.

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