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Comparing BST-CarGel® with Hyalofast for the Treatment of Hyaline Cartilage Defects

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Abstract

Objective: This study aimed to evaluate the clinical and radiological results of patients with medial femoral condyl defect who were treated with microfracture technique added with BST-CarGel® or Hyalofast as a scaffold at the end of surgery.

Methods: A total of 12 patients who had undergone microfracture surgery added with BST-CarGel® or Hyalofast as a scaffold were evaluated. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score was clinically evaluated, and the area measurement and depth and underlying structures (AMADEUS) score and defect filling were radiologically evaluated.

Results: The mean patient age was 49.66±6.31 years, and the mean follow-up time was 21.75±7.72 months. Seven patients also received BST-CarGel®, and five received Hyalofast at the end of surgery. The improvement of the WOMAC score, AMADEUS score, and defect filling after treatment were significant compared with preoperative data ($p<0.001$). No difference was found clinically and radiologically between the BST-CarGel® or Hyalofast group.

Conclusion: Microfracture treatment supplemented with BST-CarGel® or Hyalofast scaffolds at the end of surgery is a safe and helpful treatment for cartilage defects.

Keywords: Hyaline cartilage defect, microfracture, scaffold, BST-CarGel®, Hyalofast

INTRODUCTION

Cartilage lesions more commonly occur with aging. Cartilage lesions are believed to progress to degenerative osteoarthritis. Because of pain, stifness, movement limitation, decreasing quality of life, and progression to osteoarthritis, chondral defects are predisposed to surgery (1). Traditionally, hyaline cartilage surgeries can performed with osteocartilaginous replacement (2) or cartilage regeneration by autologous chondrocyte implantation (3). The advantage of these techniques are related to the use of mature autologous cartilage cells. Donor-site pathology, discontinuity in the orientation of the cartilage plugs, and fibrocartilage in the gaps are disadvantages of the osteocartilaginous replacement technique (2). Moreover, the need for two operative procedures and higher costs, are disadvantages of autologous chondrocyte implantation (4). The microfracture technique is another tratment method for chodral defects, which was described by Steadman et al. (5). This techniqe is based on bone marrow stimulation (5). The microfracture technique promotes the migration of mesenchymal stem cells for the maintainance of the cartilage in the articular surface. This techniqe forms fibrous cartilage that is not as durable as the hyaline cartilage (6).

Complications of hyaline cartilage-based surgeries and the decreased durability of the fibrous cartilage provided by the microfracture technique prompted tissue engineering professionals to strengthen the fibrous cartilage formed after microfracture. The application of scaffolds to microfracture surgery reduces this deficiency by strenghtening the quality of the formed fibrous cartilage (7,8). Of these scaffolds, BST-CarGel® (Bio-Orthopaedics Division, Piramal Life Sciences, Mumbai,

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India) stabilizes the microfracture-based blood clot by dispersing a soluble polymer scaffold containing chitosan throughout the blood and implanting the mixture over marrow access holes in a cartilage lesion (9). Another example of these scaffolds is Hyalofast (Fidia Advanced Biopolymers, Abano Terme, Italy), in which hyaluronan is one of the principal component of the articular cartilage matrix (4,10). Hyalofast promotes the release of collagen from the chondrocytes to maintain the extracellular matrix (10).

With the BST-CarGel® surgical technique, the surgeon must wait until the liquid form of the scaffold has coagulated. To achieve clotting, the defect must be paralel to the ground and the defect must allow the pooling of the liquid in the defect area during surgery. In the presence of a groove at the defect or the defect was not parallel to the ground during the clotting process, the liquid scaffold would certainly flow out of the microfracture area. However, Hyalofast is not a liquid scaffold. Thus, in our clinic, we prefer the BST-CarGel® if the defect allows pooling of the liquid scaffold. Otherwise, Hyalofast scaffold was preferred.

Because of the revealed advantage of using scaffolds, we use them in our clinic practice within its indication (1,5,6,9,11). BST-CarGel® and Hyalofast were previously compared with the microfracture technique. In this study, we aimed to present and compare the clinical and radiological results of our patients to whom these two scaffolds were added.

METHODS

The study began after it was granted permission by the Local Ethics Committee of Giresun University Giresun University Clinical Research (no: 90139838-000-E.28161, 2019-56). We retrospectively evaluated the patients who were theatened for grade 3-4 cartilage lesions of the knee joint according to the Outerbridge Arthroscopic Grading System. We investigated the patients who underwent cartilage implantation using BST-CarGel® or Hyalofast between March 2016 and March 2018 in Giresun University Hospital. The inclusion criteria, patients older than 40, patients with medial femoral condyl lesions, and patients in wom BST-CarGel® or Hyalofast was added to the microfracture surgery. The exclusion criteria were as follows: Patients with trauma, patients with additional surgeries suchas osteotomy, anterior cruciate ligament reconstruction or meniscal repair, patients with additional lesions at other surfaces of the knee, patients with rheumatic diseases, patients who have <1 year of follow-up, and patients whose data could not be reached.

For the clinical evaluation, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores were taken before surgery and at the last follow-up. For the radiologic evaluation, magnetic resonance imaging (MRI) sections which were taken before surgery and at the last follow-up were evaluated according to the area measurement and depth and underlying structures (AMADEUS) (12).

Surgical Technique

All procedures were performed under spinal anesthesia and tourniquet. Standard anterolateral and anteromedial arthroscopic portals were used. Microfracture was perfromed as previosly described (5). After obtaining the microfracture, a mini arthrotomy was performed by extending the anteromedial portal for the application of the scaffolds. The surgical techniques for BST-CarGel® (13) or Hyalofast (14) were similar as previously described. The choice of the used scaffold was based on the structure of the cartilage defect. We used the liquid BST-CarGel® if the defect allows for pooling of the fluid; otherwise, Hyalofast was used. Before all applications of the scaffolds, the microfracture area was wiped and dried with sponge via mini arthrotomy formed by extending the anteromedial arthroscopy portal. Briefly, BST-CarGel® was prepared with 4.5 mL of venous blood. Then, BST-CarGel® was injected into the microfracture area. After injection of BST-CarGel®, we waited for 15 min for the blood clot, and Hyalofast was prepared using a template of the microfacture area intraoperatively. Finally, Hyalofast was impregnated with venous blood and then placed to the microfracure area. The scaffolds were controlled in terms of stabilization after tourniquet was terminated. At the follow-up, the same rehabilitation protocol was implemented in all patients (15).

Complex meniscal tears were treated with partial meniscectomy before performing microfracture.

Evaluation of MRI

Knee MRI of patients were taken on a 1.5 Tesla MR device [MAGNETOM Aera(®); Siemens Healthcare, Erlangen, Germany]. Images for all patients were uploaded to a radiology work station (syngo.via, Siemens AG, Erlangen, Germany) on the hospital's PACS system and then evaluated. The sagital and coronal T2 images were used for measurements. The measurements were performed by the consensus of the two autors. Evaluations were made acording to AMADEUS score as previously described (12). In addition, we compared the defect filling acording to the "area measurement" criteria of the AMADEUS score.

Statistical Analysis

In this study, statistical analysis was made by using "SPSS Statistics version 23 (IBM Corp., NY, USA)". The Shapiro-Wilk test

was used to test for the normality of the variables. Independent samples t-test and paired sample t-tests were used to compare the means. Arithmetic mean and standard deviations were used as descriptive statistics. Besides, an alpha of 0.05 was used as the cutoff for significance.

RESULTS

Between March 2016 and March 2018, 12 (7 male, 5 female) patients had received microfracture treatment at medial femoral condyl with BST-CarGel® or Hyalofast. The mean age of all patients were 49.66±6.31 years, with a mean follow-up duration 21.75±7.72 months. No significant difference was found according to independent sample t-test applications [sig. (p)=0.843>0.01 and sig. (p)=0.937>0.01, respectively] between the BST-CarGel® and Hyalofast groups in terms of their mean age [BST-CarGel®: 49±6.48 (n=7) year, Hyalofast: 50.6±6.69 (n=5)] and follow-up duration (BST-CarGel®: 22±8.10 months; Hyalofast: 21.4±8.08 months). The clinical and radiological data of the patients are given in Table 1. MRI sections are shown at Figure 1.

The preoperative and postoperative changes in the WOMAC score, radiological AMADEUS score, and defect filling of all patients are separately analyzed with the paired samples t-test, because each data set has normal distrbution and interdependence. In the test carried out according to the 5% significance level of paired samples, the sig values for each pair are <0.05 (0.000<0.05). The progression in the WOMAC score, radiological AMADEUS score, and defect filling at the last follow-up were significant according to the paired sample t-test applications in all patients (p<0.001; p<0.001; p<0.001, respectively; Table 1).

The preoperative and postoperative changes in the WOMAC score, radiological AMADEUS score, and defect filling of the BST-CarGel® goup were separately analyzed with the paired samples t-test, because each data set has normal distrubtion and interdependence. In the test carried out according to the 5% significance level of the paired samples, the sig values of for each pair were <0.05. The increase in the WOMAC score, radiological AMADEUS score, and defect filling at the last follow-up were significant according to the paired sample t-test applications in the BST-CarGel® group (p<0.001; p<0.001; p<0.01, respectively; Table 1).

The preoperative and postoperative changes in the WOMAC score, radiological AMADEUS score, and defect filling of the Hyalofast group were separately analyzed with the paires samples t-test, because each data set has a normal distrubtion and interdependence. In the test performed according to the 5% significance level of te paired samples, the sig. values of for each pair are <0.05. The progress of the WOMAC score, radiological

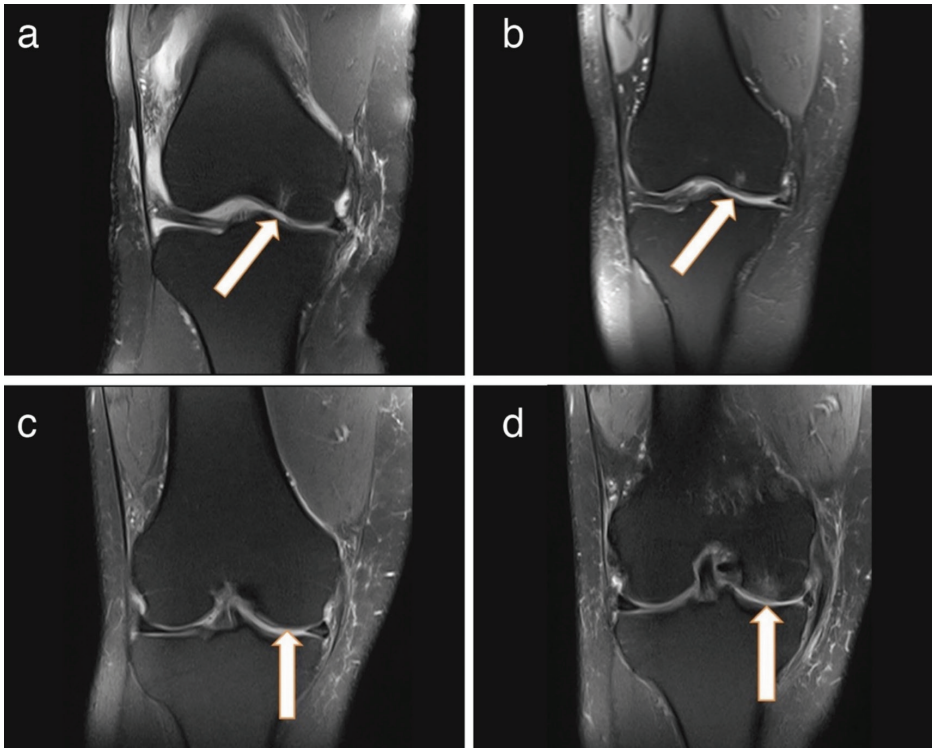

Figure 1. (a, b) Hyalofast group. (c, d) BST-CarGel® group. (a, c) Preoperative sections; arrows indicate the cartilage defected area. (b, d) Postoperative sections; arrows indicate the thickening of the healed cartilage

AMADEUS score, and defect filling at last follow-up were significant according to the paired sample t-test applications in the Hyalofast group ($p<0.01$; $p<0.001$; $p<0.01$, respectively; Table 1).

The preoperative and postoperative differences in the WOMAC score or radiological AMADEUS score or defect filling between the BST-CarGel® group and Hyalofast group were analyzed with the independent sample t-test separately, because each data set has normal distrubtion and independence of each other. In Table 1, in the analysis performed according to the 5% significance level, all p values were <0.05 for comparisons. According to statistical test results, no significant difference was found betwen the means of preoperative and postoperative data between the BST-CarGel® group and Hyalofast group ($p>0.05$; Table 1).

Of all patients, nine had complex meniscal tear at the medial menisci. Complex meniscal tears were treated via partial meniscectomy.

DISCUSSION

In this study, we investigated the results of patients who were treated by the microfracture technique and suppplemented with BST-CarGel® or Hyalofast scaffolds at the end of the surgery. The WOMAC clinic score and radiological AMADEUS score before surgery and at the last follow-up showed a significant improvement ($p<0.001$) (Table 1). The preoperative and postoperative comparisons of BST-CarGel® and Hyalofast groups were not significant according to the WOMAC score, radiological AMADEUS score, and defect filling ($p>0.05$) (Table 1).

Stanish et al. (1) presented the clinic and radiologic results of patients who received BST-CarGel® and isolated microfracture. Of their 80 patients, 40 were treated by microfracture only, and the remaining 40 received BST-CarGel®. All patients clinically improved in their series compared with their preoperative condition. No significant clinical difference was found the between groups according to the WOMAC score. The BST-CarGel® group had better radiological improvement according to MRI. Shive et al. (9) published their experience with BST-CarGel® compared with isolated microfracture in 2015. Microfracture with and without BST-CarGel® showed superiority compared with preoperative conditions. The clinical and radiological results of Shive et al. (9) were similar with those of Stanish et al. (1). Buda et al. (4) presented the results of patients with microfracture added with Hyalofast. They found similar results to Stanish et al. (1) and Shive et al. (9) in terms of clinical improvement. In the current study, we found radiological and cilinical progress preoperatively to postoperatively, as in the literature.

The use of scaffolds probably helps mesenchymal stem cells to differentiate to more durable cartilage (10). The histological studies of Hyalofast (4,10) and BST-CarGel® (11) at cartilage repair showed a more durable cartilage repair. The clinical success achieved may be due to the microfracture treatment and/or the scaffolds used. Clinical studies that compared microfracture treatment with and without scaffolds showed the same clinic improvement, but the scaffold groups showed

Tablo 1. Clinic and radiological outcomes of the patients

		All patients (BST-CarGel® + Hyalofast) (n=12)	BST-CarGel® group (n=7)	Hyalofast group (n=5)	[a]p
		Mean ± SD	Mean ± SD	Mean ± SD	
AMADEUS	Preoperative	56.18±6.68	54.28±7.86	54±5.47	**0.946**
	Postoperative	83.75±8.56	81.42±8.99	87±7.58	**0.287**
	Δ AMEDEUS difference	-29.58±8.38	-27.14±7.55	-33.00±9.08	-
	[b]p	**<0.000****	**<0.000****	**0.001****	-
WOMAC	Preoperative	29.26±10.77	28.91±13.47	29.76±6.79	**0.901**
	Postoperative	89.89±4.71	89.98±4.01	89.76±6.07	**0.939**
	Δ WOMAC difference	60.62±10.92	-61.07±13.60	-60.00±7.05	-
	[b]p	**<0.000****	**<0.000****	**<0.000****	-
Defect filing	Preoperative	2.24±0.95	2.35±1.12	2.1±0.73	**0.664**
	Postoperative	0.88±0.28	0.89±0.3	0.85±0.29	**0.811**
	Δ Defect filing difference	1.36±0.70	1.45±0.86	1.24±0.47	-
	[b]p	**<0.000****	**0.004****	**0.004****	-

[a]Independent samples test, [b]Paired samples test, **p<0.0, SD: Standard deviation, AMADEUS: Area measurement and depth and underlying structures, WOMAC: The Western Ontario and McMaster Universities Osteoarthritis Index

better radiological improvement. BST-CarGel® and Hyalofast do not only induce the quality of fibrous cartilage but also increase the amount of filling in the defected area (1,4,10,11). Previous studies have demonstrated the increased quality of the newly formed fibrous cartilage and increased clinical satisfactory with BST-CarGel® or Hyalofast (1,4,13,16-18). These studies have presented short- and mid-term results (1,4,9,11,16-18). We believe that the major clinical reflection of these studies would be seen in the long-term. Recently, Solheim et al. (19) compared the long-term results of OATS and microfracture. Solheim et al. (19) reported that the survival of the hyaline cartilage-based treatment OATS is better than the fibrous cartilage-based treatment with the microfracture technique. However, as the clinical, radiological, and histological studies of Hyalofast or BST-CarGel® for cartilage repair showed more durable cartilage repair (1,4,6,9-11), the follow-up durations of the aforementioned studies are still shorter than that of hyaline-based treatments (19). The studies put forth the improvement at the filling of the cartilage defect in the scaffold group compared with the microfracture group, despite the lack of difference in the clinic outcomes between the groups (1,9,11). Thus, studies have presented the long-term results of patients who used scaffolds (1,4,9,11).

Therefore, cartilage scaffolds are not only used in the knee. Some studies have shown the superity of the cartilage scaffolds for hyaline cartilage defects in the synovial joints other than in the knee joint (20-22). The success of adding scaffolds at the lower extremity cartilage repair (1,4,9,11,20-22) can put forth the importance of increased quality of repair tissue. Scaffolds serve as a plug at the microfracture area. Moreover, the scaffolds may provide the same height level between the clot and the healthy hyaline cartilage border.

The most important difference of our study group from the literature is the application of Hyalofast with venous blood instead of mesenchymal stem cells obtained from the iliac crest as in the routine technique. The phenotype and differentiation potential of the cells at the distal femur are similar to those of bone marrow-derived mesenchymal stem cells from the iliac crest (23). Thus, we targeted the benefit of stem cells in those who come by microfracture surgery. Thus, a less invasive technique was applied to the patients. In the BST-CarGel® technique, venous blood is used routinely. The use of the venous blood for the scaffolds made the approaches of BST-CarGel® and Hyalofast more similar to eachother. Thus, the techniques were similar as much as possible, except for the used scaffolds. The tourniquet was removed after the scaffold-supported plugs hardened. In terms of instability of the used scaffolds, such as separation from the microfracture area, we controlled every case intraoperatively after terminating the tourniquet. The incision was closed after being sure of the stability of the used scaffolds.

Study Limitations

The limitations of this study are on the low sample size, short follow-up time, and lack of histological results. Another important limitation is the lack of microfracture only group. Because the superiority of adding scaffolds to the microfracture treatment was shown previously, we have not included any patient group in which microfracture was performed alone.

CONCLUSION

The addition of BST-CarGel® or Hyalofast to microfracture surgery is beneficial clinically and radiologically. To compare the long-term results of these two scaffolds with microfracture alone and/or hyaline cartilage-based treatment, further studies are needed.

Ethics

Ethics Committee Approval: The study began after it was granted permission by the Local Ethics Committee of Giresun University Giresun University Clinical Research (no: 90139838-000-E.28161, 2019-56).

Informed Consent: Informed consent form was obtained from all patients.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: K.A., C.Z.E., Design: K.A., C.Z.E., Data Collection or Processing: K.A., C.Z.E., Analysis or Interpretation: K.A., C.Z.E., Literature Search: K.A., C.Z.E., Writing: K.A., C.Z.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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