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Research Article

Midterm Clinical Outcome of Single-Stage Knee Articular Cartilage Repair Using Hyaluronic Acid-Based Scaffold Embedded with Bone Marrow Aspirate Concentrate (HA-BMAC) Combined with Microfracture

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Abstract

Introduction: Single-stage knee articular cartilage repair using Hyaluronic Acid-based scaffold embedded with bone marrow aspirate concentrate combined with microfracture (HA-BMAC-microfracture) is a significant advancement in the treatment of chondral injury.

Objectives: To investigate the midterm clinical outcome of knee cartilage repair treated with HA-BMAC-microfracture.

Methods: Clinical outcomes were assessed via patient-reported scoring tools, namely the International Knee Documentation Committee (IKDC), subjective function score (Lysholm score), ability to return to sports and performing daily prayers in a normal manner. They were assessed preoperative, at short-term follow-up (1 year and 2 years postoperative), and at mid-term follow-up (4 years postoperative).

Results: Twenty-four patients fulfilled the criteria, mean age 36.7 years. Mean IKDC score showed statistically significant (P value < 0.001) increase from preoperative to 1year postoperative (65.2), from preoperative to 2 years postoperative (62.6) and from preoperative to 4years postoperative (58.2). Lysholm score also showed statistically significant (P value < 0.001) increase from preoperative to 1 year postoperative (56.6), from preoperative to 2 years postoperative (54.9), and from preoperative to 4 years postoperative (46.5). On the ability to return to sports also showed statistically significant outcomes. From preoperative to 1 year postoperative (P value 0.031), to 2 years postoperative (P value 0.031) and to 4 years postoperative (P value 0.031). However, the proportion of return to sports from 1 year to 2 years postoperative (P = 1.00), to 4years post operative (P = 1.00) and from 2 years to 4 years postoperative (P = 1.00) was not statistically significant. Similarly, the proportion of individuals able to perform daily prayers in a normal manner also showed statistically significant improvement. From preoperative to 1 year postoperative (P value 0.021), to 2 years postoperative (P value 0.008), and to 4 years postoperative (P value 0.008). There was no significant difference in the proportion of prayer outcomes from 1 year to 2 years postoperative (P value 1.00), to 4 years postoperative (P value 1.00) and from 2 years to 4 years postoperative (P value 1.00).

Conclusion: HA-BMAC-microfracture for the treatment of knee cartilage injury provides a good clinical outcome at short and midterm follow up. Despite good clinical outcome, none of the patients were able to return to pre- injury level sports and all patients with patellofemoral lesion did not return to praying normally.

Keywords: Chondral Injury; Biological Scaffold; Hyaluronic Acid Scaffold; Bone Marrow Aspirate Concentrate; Platelet- Rich Plasma; HA-BMAC

What are the New Findings?

- HA-BMAC-microfracture for the treatment of knee cartilage injury provides a good clinical outcome at short and mid- term follow up.
- Despite good outcome, none of the patients were able to return to pre- injury level of sports.
- All patients with patellofemoral lesion did not return to praying normally (kneeling with deep knee flexion).

Introduction

Knee chondral injuries are difficult to treat entities affecting all age group. Its treatment remains a clinical challenge especially large full thickness lesion. Cartilage has limited intrinsic healing potential because it is hypocellular, avascular, aneural and non-lymphatic, thus diminishing the capacity of tissue regeneration [1,2,4]. Injury to articular cartilage is prevalent and leads to cartilage degeneration and early osteoarthrosis [3]. This condition can be debilitating due to chronic long-standing knee pain, functional disability and reduced quality of life. Significant morbidity from this has led to continuous evolution of cartilage injury management [3].

Current concept of a single stage cartilage repair technique with Hyaluronic-based scaffold implantation embedded with bone marrow derived cells with or without bone marrow stimulation technique is being practiced worldwide [4,6,12,14,15]. Placement of this biological scaffolds soaked with bone marrow derived cells over the cartilage defect following microfracture provides a mechanically stable structure for repair to take place. This acts as a biocompatible temporary scaffold that concentrates the mesenchymal cells and growth factors over the area of defect [10-13].

To date there is no clinical data on the outcome of patients treated with HA-BMAC-microfracture in Malaysia. Thereby this study is aimed to investigate the midterm clinical outcome of single stage HA-BMAC-microfracture for the treatment of knee cartilage injury. Ethics approval was granted by the national review board.

Methods

Data collection

Patients who underwent knee cartilage lesion treatment with HA-BMAC-microfracture at the Arthroscopy and Sports Injury Unit Department of Orthopedic, Hospital Kuala Lumpur, Malaysia, between October 2013 and December 2017 were reviewed in this study. The inclusion criteria were a minimum follow up of 4 years, patients aged 18 to 45 years with symptomatic articular cartilage defects classified as International Cartilage Repair Society (ICRS) grade III and above, localized to a single compartment of the knee (medial compartment, patellofemoral compartment and lateral compartment), chondral lesion size of > 2 cm^2 in diameter, body mass index (BMI) < 30 kg/m^2. Magnetic Resonance Imaging was routinely used pre-operatively to assess the lesion and confirmed by a diagnostic arthroscopy before cartilage lesion repair. Patients were excluded if they had general systemic illness, known history of autoimmune or inflammatory arthritis, intra articular steroid injections, neurovascular disease, tri compartmental osteoarthritis, < 18 or > 45 years of age, more than single compartment involvement, cartilage defects classified as International Cartilage Repair Society (ICRS) grade II and lower and incomplete or insufficient follow-up data.

Patients-reported assessment tools were used preoperatively, at short-term follow-up (1 year and 2 years postoperatively), and at mid-term follow-up (4 years postoperatively) to examine the clinical outcome. Tools consisted of the International Knee Documentation Committee (IKDC) [17,23], subjective function score (Lysholm score), the abilities of patients return to sports and performing daily prayers in a normal manner (which requires kneeling and sitting down on the floor with deep knee flexion).

Pre-operative reports and intra operative reports were reviewed to better characterize the articular cartilage lesions in terms of location, size in millimeters and ICRS grading. To better define the location of the defects the knee was further numbered and defined by a 3 x 3 grid and the femoral condyle was divided into thirds (medial, central and lateral) as per validated ICRS grid map. Figure 1- supplementary information [16] illustrates the grid distribution.

Surgical technique

All surgical procedures were performed by sports-trained surgeon. The patient was positioned supine with operative knee and the ipsilateral iliac crest were included in the sterile field of preparation. The surgical procedure begins with a routine diagnostic scope to confirm the suitability for HA-BMAC with microfracture

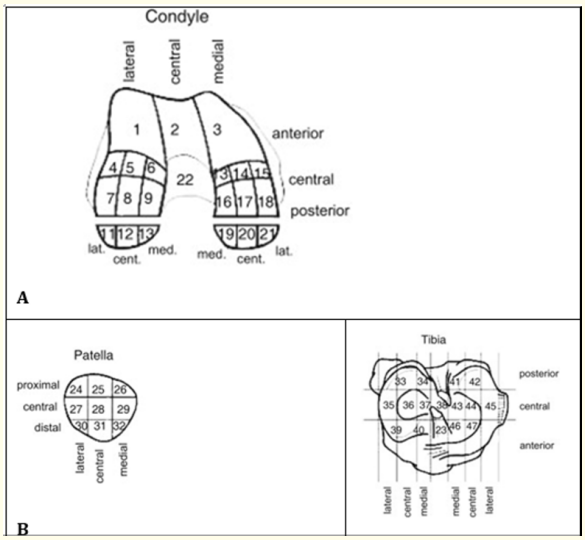

Figure S1: Grid distributions for the femoral condyles (A), patella (B) and the tibia (C).

cartilage repair. Associated procedures were performed as indicated before proceeding with any cartilage work. A 60 ml volume of bone marrow aspirate was obtained from the ipsilateral iliac crest with a standardized kit and processed in a commercially available system (BMAC harvest system) to isolate bone marrow aspirate with a total nucleated marrow cell concentration approximately 6 times the baseline concentration.

Once the defect was confirmed and measured, the lesion was debrided with an arthroscopic shaver and a curette. If the defect especially patella defects which are difficult to address via arthroscopically then a mini arthrotomy was performed. All unstable chondral fragments were removed. Lesions were prepared by creating vertical cartilage walls peripherally around each defect creating a stable shoulder. The defect base was debrided uniformly to remove the calcified cartilage layer without violating the subchondral plate.

Post debridement measurement of the lesion is done in order to template its dimension to match the size of hyaluronic acid-based scaffold. The activated BMAC clot was implanted onto the scaffold. Microfractures was performed using a 1 mm Kirschner wires drilled at approximate regular 5 mm intervals to induce bleeding from the defect site. Finally, the shaped scaffold along with activated BMAC is placed over the defect after microfractures. The scaffold was subsequently allowed to stabilize before checking for its stability via repeatedly cycling of the knee through a full range of flexion and extension during direct visualization of the repair sites. The surgical procedure is illustrated in figure 1.

Figure 1: Surgical technique.

Rehabilitation protocol

Post-operative rehabilitation was done in our centre by trained physiotherapist who follows our standard planned rehab protocol. All patients went thru a standard rehabilitation protocol customised to the location of the cartilage defects supervised by a trained physiotherapist. The aim is to allow gradual return to weight bearing without destabilizing the hyaluronic acid-based scaffold by avoiding unnecessary compressive and shearing forces.

The initial 6 weeks is focused on pain control, resolution of effusion and minimizing muscular atrophy. In terms of range of motion and weight bearing, if the defect was located at a weightbearing surface, patients were advised to immobilize the knee in extension and non-weight bearing for 6 weeks followed by partial weight bearing with increasing range of motion. Active and passive range of motion exercises as well as isometric quadriceps exercises were started day one post operatively however maximum knee flexion did not exceed the destabilising degree noted intra operatively, until the end of the 4th week after surgery.

Statistical analysis

Data analysis was executed with SPSS, Statistical Package for the Social Sciences (SPSS) version 24 (IBM Corp., Armonk, NY). This study will give results of pre- and post-operative functional outcome (1 year, 2 years and 4 years post-operatively) of the knee following using single stage cartilage repair technique via Hyaluronic- based scaffold implantation embedded with bone marrow derived cells combined microfracture procedure with respect to IKDC score, subjective function score (Lysholm) score, return to sports and return to performing daily prayers in a normal manner.

Normality of continuous variables was evaluated with quantile-quantile plots and the Shapiro-Wilk test. Results are presented as means with standard deviations for continuous variables and percentages for categorical variables of the total number of knees in the entire patient group. The Wilcoxon signed- rank test was used for continuous data, whereas McNemar's test was employed for categorical data to examine the differences among pre- and post-operative functional outcome of the knee assessment tools.

Differences in scores among categories of socio demographics which consist of age, lesion size, compartment involvement and associated injuries were compared with the Mann- Whitney U test for two independent variables and the Kruskal-Wallis test for three or more independent variables. Association between functional outcome scores and the socio demographics of ages, BMI, lesion size, compartment involvement and associated injuries were examined with Spearman rank correlation analysis. In this study, comparative analysis 2 tailed was used, and the statistical significance was defined as $P < 0.05$.

Results

Demographic data

A total of 54 patients who underwent knee cartilage lesion treatment with HA-BMAC-microfracture at the Arthroscopy and Sports Injury Unit Department of Orthopaedic, Hospital Kuala Lumpur were collected in this study. Out of them, 24 patients met the inclusion criteria and were analyzed in this study. Basic demographic information including age, gender, ethnicity, height, weight, BMI, type of sport activities, the effected knee, mode injury, type of surgery, compartments of the knee involved and any concurrent injuries are detailed in table 1-supplementary information.

Characteristics	Value
Age (years)	36.7 ± 7.2
Height (cm)	164.2 ± 6.7
Weight (kg)	67.0 ± 9.4
BMI	24.8 ± 2.5
Gender	
Male	13 (54.2)
Female	11 (45.8)
Ethnicity	
Malay	22 (91.7)
Chinese	2 (8.3)
Mode Injury	
Fall	15 (62.5)
Sports	7 (29.2)
MVA	2 (8.3)
Affected Knee	
Right	10 (41.7)
Left	14 (58.3)
Type of Sport Activities	
Competitive	8 (33.3)
Leisure	16 (66.7)
Type of Surgery	
Arthroscopic assisted	18 (75.0)
Mini Open	6 (25.0)
Compartment involved for surgery	
Lateral	7 (29.2)
Medial	11 (45.8)
Patellofemoral	6 (25.0)
Associated injuries	
No	9 (37.5)
Yes	15 (62.5)
ACL	4 (26.7)
Meniscus tear	3 (20.0)
MPFL	4 (26.7)
ACL and Meniscus tear	3 (20.0)
MPFL and Meniscus tear	1 (6.6)

Table S1: Patient demographics and clinical findings.

Data are mean ± standard deviation or n (%). Abbreviations: ACL: Anterior Cruciate Ligament; MPFL: Medial Patella Femoral Ligament.

Of the 24 knees analysed in this study, 18 patients (75.0%) had undergone arthroscopic assisted surgery and 6 patients (25.0%) had undergone mini open surgery. There are 9 patients (37.5%) who do not have associated injuries whereas 15 patients (52.5%) have associated injuries which comprises injuries of ACL (4), meniscus tear (3), MPFL (4), ACL and meniscus tear (3), MPFL and meniscus tear (1) respectively. They underwent a concurrent arthroscopic procedure in the same setting for an ACL reconstruction, MPFL reconstruction and meniscus repair, debridement or meniscectomy. Table 2-supplementary information shows the descriptive data of cartilage lesions.

Anatomic Location	Frequency	Mean of ICRS Grade
Lateral femoral condyle		
2	1	4
3	1	4
4	1	4
5	2	4
7	2	4
8	6	4
9	3	3
12	1	3
Medial femoral condyle		
14	5	4
16	1	4
17	11	4
18	8	4
20	4	4
Patellofemoral femoral condyle		
27	3	4
28	6	4
29	3	3
32	1	3

Table S2: Characteristics of articular cartilage lesions.

Based on preoperative imaging and intra-operative findings, articular cartilage lesions are described according to their location and mean International Cartilage Repair Society (ICRS) grade. Specific locations of the lesions are detailed in figure 1.

Postoperative outcomes

The data results for the postoperative outcomes for IKDC and Lysholm score are summarized in table 1.

The mean IKDC score showed statistically significant increase from pre-op to 1-year post op (65.2), from pre-op to 2 years post op (62.6) and from pre-op to 4 years post op (58.2). A Wilcoxon-signed rank test showed that the clinical outcomes for IKDC scores between each of interval assessments elicit a statistically significant change with the P value < .001.

Similarly, the Lysholm score showed statistically significant increase from pre-op to 1-year post op (56.6), from pre-op to 2 years post op (54.9), and from pre-op to 4 years post op (46.5). The results from Wilcoxon signed-rank test done on clinical outcomes for Lysholm scores between each of interval assessments evoke a statistically significant change with the P value < .001.

Scores				
	Pre-Op	**1 year**	**2 years**	**4 years (Final)**
IKDC score	18.3 ± 7.9	83.5 ± 11.8	80.9 ± 12.1	76.5 ± 16.2
Lysholm	35.0 ± 7.6	91.6 ± 6.4	89.9 ± 7.2	81.5 ± 20.0

P Values					
Pre-Op vs 1 y	**Pre-Op vs 2 y**	**Pre-Op vs 4 y (Final)**	**1 y vs 2 y**	**1 y vs 4 y (Final)**	**2 y vs 4 y (Final)**
< 0.001[b]	< 0.001[b]	< 0.001[b]	< 0.001[b]	< 0.001[b]	< 0.001[b]
< 0.001[b]	< 0.001[b]	< 0.001[b]	< 0.001[b]	< 0.001[b]	0.001[b]

Table 1: Comparison of clinical outcomes of IKDC and Lysholm scores between each interval assessment.

[a] Scores are listed as mean ± standard deviation. Abbreviations: IKDC: International Knee Documentation Committee.

[b] Statistically significant, P < 0.05.

Table 2 represent the postoperative outcome for patient's ability to perform the prayers in normal manner (kneeling on knees in deep flexion). An exact McNemar's test implied that that there was a statistically significant difference in the proportion of prayer outcomes from pre op to 1-year post op (P = 0.021), to 2 years post op (P = 0.008), and to 4 years post op (P = 0.008). However, there were no significant difference in the proportion of prayer outcomes from 1 year to 2 years post op (P = 1.00), to 4 years post op (P = 1.00) and from 2 years to 4 years post op (P = 1.00).

		Prayers		
	Pre-Op	**1 year**	**2 years**	**4 years (Final)**
Abnormal	22 (91.7)	15 (62.5)	14 (58.3)	14 (58.3)
Normal	2 (8.3)	9 (37.5)	10 (41.7)	10 (41.7)

P Values					
Pre-Op vs 1 y	**Pre-Op vs 1 y**	**Pre-Op vs 1 y**	**Pre-Op vs 1 y**	**Pre-Op vs 1 y**	**Pre-Op vs 1 y**
0.021[b]	0.021[b]	0.021[b]	0.021[b]	0.021[b]	0.021[b]

Table 2: Comparison of prayer outcomes between each interval assessment.

[a] Scores are listed as n (%).

[b] Statistically significant, P < 0.05.

Table 3 is the result for postoperative outcomes for patient's ability to return to sports. All patients after their injury were never able to go back to their sports activities. However, some went back to sports after surgery but was never able to return to their pre-injury level of sports. An exact McNemar's test indicate that there was a statistically significant difference in the proportion of return to sports outcomes from pre op to 1-year post op (P = 0.031), to 2 years post op (P = 0.031), and to 4 years post op (P = 0.031). However, the proportion of return to sports outcomes from 1 year to 2 years post op (P = 1.00), to 4 years post op (P = 1.00) and from 2 years to 4 years post op (P = 1.00) did not elicit a statistically significant change.

		Return to Sports		
	Pre-Op	**1 y**	**2 y**	**4 y (Final)**
Yes		6 (25.0)	6 (25.0)	6 (25.0)
No	24 (100.0)	18 (75.0)	18 (75.0)	18 (75.0)

P Values					
Pre-Op vs 1 y	**Pre-Op vs 2 y**	**Pre-Op vs 4 y (Final)**	**1 y vs 2 y**	**1 y vs 4 y (Final)**	**2 y vs 4 y (Final)**
.031[b]	.031[b]	.031[b]	1.000[b]	1.000[b]	1.000[b]

Table 3: Comparison of return to sport outcomes between each interval assessment.

[a] Scores are listed as n (%).

[b] Statistically significant, P < .05.

Descriptive statistics for final postoperative outcome for patients' ability return to sport based on age, lesion size, compartment involved, and associated injuries are outlined based on table 4.

	Return to sport	
	Yes	**No**
Age		
< 40 years old	5	10
≥ 40 years old	1	8
Lesion Size		
< 4 cm^2	5	12
≥ 4 cm^2	1	6
Compartment Involvement		
Lateral	4	3
Medial	2	9
Patellofemoral		6
Associated injuries		
No	2	7
Yes	4	11

Table 4: Patient's ability return to sport for postoperative outcomes at final follow-up (4 years).

A Mann-Whitney test was used to evaluate the differences in functional outcome scores among categories of age group, lesion size and associated injuries, whereas Kruskal-Wallis H test was used to examine the differences in functional outcome scores of compartment involvement. Results illustrated in table 5.

	Age		
	< 40 y (n = 15)	**≥ 40 y (n = 9)**	**P value**
IKDC Scores	81.6 ± 12.8	68.0 ± 18.5	.060
Lysholm Scores	83.5 ± 22.3	78.2 ± 16.1	.128
Prayers			
Normal	8 (53.3%)	2 (22.2%)	.143
Abnormal	7 (46.7%)	7 (77.8%)	
Return to Sports			
Yes	5 (33.3%)	1 (11.1%)	.233
No	10 (66.7%)	8 (88.9%)	

	Lesion Size		
	< 4 cm² (n = 17)	**≥4 cm² (n = 7)**	**P value**
IKDC Scores	76.6 ± 17.3	76.2 **± 14.8**	.703
Lysholm Scores	79.9 ± 22.7	85.4 **± 11.6**	.899
Prayers			
Normal	7 (41.2%)	3 (42.9%)	.941
Abnormal	10 (58.8%)	4 (57.1%)	
Return to Sports			
Yes	5 (29.4%)	1 (14.3%)	.446
No	12 (70.6%)	6 (85.7%)	

	Associated Injury		
	No (n = 9)	**Yes (n = 15)**	**P value**
IKDC Scores	76.5 ± 14.8	76.5 ± 17.5	.835
Lysholm Scores	85.3 ± 11.5	79.3 ± 23.8	.952
Prayers			
Normal	4 (44.4%)	6 (40.0%)	.834
Abnormal	5 (55.6%)	9 (60.0%)	
Return to Sports			
Yes	2 (33.3%)	4 (66.7%)	.812
No	7 (38.9%)	11 (61.1%)	

		Compartment Involvement		
	Lateral (n = 7)	**Medial (n = 11)**	**Patellofemoral (n = 6)**	**P value**
IKDC Scores	85.9 ± 9.6	76.4 ± 15.5	65.6 ± 18.9	.134
Lysholm Scores	81.1±31.9	85.5 ± 11.4	74.8 ± 16.4	.260
Prayers				
Normal	5 (71.4%)	5 (45.5%)		.037
Abnormal	2 (28.6%)	6 (54.5%)	6 (100%)	
Return to Sports				
Yes	4 (57.1%)	2 (18.2%)		.053
No	3 (42.9%)	9 (81.8%)	6 (33.3%)	

Table 5: Clinical outcomes scores at mean final follow-up of 4 years by age group, lesion size, associated injury and compartment involvement.

[a] Scores are listed as mean ± standard deviation or n (%).

Abbreviations: IKDC: International Knee Documentation Committee.

[b] Statistically significant, P < .05.

Comparative analysis of patients grouped by age below 40 years old or 40 years old and above did not demonstrate any significant differences in final outcome scores (P > .05). Similarly, patient grouped by treated lesion size < 4 cm^2 and ≥ 4 cm^2 also was statistically insignificant (P > .05). Likewise, there were also no significant differences in final outcome scores for those patients who have any associated injuries (P > .05). IKDC, Lysholm scores and abilities patients to return to sport shows no significant differences towards compartment involvement (P > .05). However, clinical outcomes for patient's ability to perform the prayers in normal manner had significant differences with p value 0.037. Thus, it can be concluded that the clinical outcome of to perform prayers has significant difference with respect to the compartment involved.

Spearman's rank correlation analysis was tested in order to assess the monotonic relationship between socio demographic which comprises age, BMI, lesion size, any associated injuries and compartment involvement with respected to functional outcome. Correlation analysis demonstrated a significantly negative correlation of patient age and final outcome scores according to IKDC (rs = -.427, P = .037), Lysholm scores (rs = -.354, P = .040), prayers (rs = -.286, P = .044) and return to sports (rs = -.361 P = .050). There are no significant correlations were identified between any final outcomes score respected to socio demographics which comprised of BMI, lesion size, compartment involvement, associated injuries (Refer to Appendix 1- supplementary information).

Appendix 1

Correlation functional outcomes of IKDC and Lysholm scores, patient abilities to perform the prayers and return to sports respected to age

			Age	**IKDC score**
Spearman's rho	Age	Correlation coefficient	1.000	-.427
		Sig. (2 tailed)	.	.037
		N	24	24
	IKDC scores	Correlation coefficient	-.427	1.000
		Sig. (2 tailed)	.037	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			Age	Lysholm score
Spearman's rho	Age	Correlation coefficient	1.000	-.354
		Sig. (2 tailed)	.	.040
		N	24	24
	Lysholm scores	Correlation coefficient	-.354	1.000
		Sig. (2 tailed)	.040	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			Age	Prayers
Spear-man's rho	Age	Correlation coefficient	1.000	-.286
		Sig. (2 tailed)	.	.044
		N	24	24
	Prayers	Correlation coefficient	-.286	1.000
		Sig. (2 tailed)	.044	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			Age	Return to Sports
Spear-man's rho	Age	Correlation coefficient	1.000	-.361
		Sig. (2 tailed)	.	.050
		N	24	24
	Return to Sports	Correlation coefficient	-.361	1.000
		Sig. (2 tailed)	.050	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

Correlation functional outcomes of IKDC and Lysholm scores, patient abilities to perform the prayers and return to sports respected to BMI

			BMI	IKDC score
Spearman's rho	BMI	Correlation coefficient	1.000	.044
		Sig. (2 tailed)	.	.838
		N	24	24
	IKDC scores	Correlation coefficient	.044	1.000
		Sig. (2 tailed)	.838	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			BMI	Lysholm score
Spearman's rho	BMI	Correlation coefficient	1.000	.290
		Sig. (2 tailed)	.	.169
		N	24	24
	Lysholm scores	Correlation coefficient	.290	1.000
		Sig. (2 tailed)	.169	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			BMI	Prayers
Spearman's rho	BMI	Correlation coefficient	1.000	.024
		Sig. (2 tailed)	.	.910
		N	24	24
	Prayers	Correlation coefficient	.024	1.000
		Sig. (2 tailed)	.910	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			BMI	Return to Sports
Spearman's rho	BMI	Correlation coefficient	1.000	-.028
		Sig. (2 tailed)	.	.897
		N	24	24
	Return to Sports	Correlation coefficient	-.028	1.000
		Sig. (2 tailed)	.897	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

Correlation functional outcomes of IKDC and Lysholm scores, patient abilities to perform the prayers and return to sports respected to lesion size

			Lesion Size	IKDC score
Spearman's rho	Lesion Size	Correlation coefficient	1.000	.079
		Sig. (2 tailed)	.	.712
		N	24	24
	IKDC scores	Correlation coefficient	.079	1.000
		Sig. (2 tailed)	.712	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			Lesion Size	Lysholm score
Spearman's rho	Lesion Size	Correlation coefficient	1.000	-.027
		Sig. (2 tailed)	.	.902
		N	24	24
	Lysholm scores	Correlation coefficient	-.027	1.000
		Sig. (2 tailed)	.902	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			Lesion Size	Prayers
Spearman's rho	Lesion Size	Correlation coefficient	1.000	.015
		Sig. (2 tailed)	.	.943
		N	24	24
	Prayers	Correlation coefficient	.015	1.000
		Sig. (2 tailed)	.943	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			Lesion Size	Return to Sports
Spearman's rho	Lesion Size	Correlation coefficient	1.000	.159
		Sig. (2 tailed)	.	.459
		N	24	24
	Return to Sports	Correlation coefficient	.159	1.000
		Sig. (2 tailed)	.459	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

Correlation functional outcomes of IKDC and Lysholm scores, patient abilities to perform the prayers and return to sports respected to compartment involvement

			C.I	IKDC score
Spearman's rho	C.I	Correlation coefficient	1.000	-.121
		Sig. (2 tailed)	.	.574
		N	24	24
	IKDC scores	Correlation coefficient	-.121	1.000
		Sig. (2 tailed)	.574	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			C.I	Lysholm score
Spearman's rho	C.I	Correlation coefficient	1.000	-.144
		Sig. (2 tailed)	.	.503
		N	24	24
	Lysholm scores	Correlation coefficient	-.144	1.000
		Sig. (2 tailed)	.503	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			C.I	Prayers
Spearman's rho	C.I	Correlation coefficient	1.000	.263
		Sig. (2 tailed)	.	.215
		N	24	24
	Prayers	Correlation coefficient	.263	1.000
		Sig. (2 tailed)	.215	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			C.I	Return to Sports
Spearman's rho	C.I	Correlation coefficient	1.000	-.045
		Sig. (2 tailed)	.	.835
		N	24	24
	Return to Sports	Correlation coefficient	-.045	1.000
		Sig. (2 tailed)	.835	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

Correlation functional outcomes of IKDC and Lysholm scores, patient abilities to perform the prayers and return to sports respected to associated injuries

			AI	IKDC score
Spearman's rho	AI	Correlation coefficient	1.000	.044
		Sig. (2 tailed)	.	.840
		N	24	24
	IKDC scores	Correlation coefficient	.044	1.000
		Sig. (2 tailed)	.840	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			AI	Lysholm score
Spearman's rho	AI	Correlation coefficient	1.000	.012
		Sig. (2 tailed)	.	.954
		N	24	24
	Lysholm scores	Correlation coefficient	.012	1.000
		Sig. (2 tailed)	.954	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			AI	Prayers
Spearman's rho	AI	Correlation coefficient	1.000	.044
		Sig. (2 tailed)	.	.840
		N	24	24
	Prayers	Correlation coefficient	.044	1.000
		Sig. (2 tailed)	.840	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

			AI	Return to Sports
Spearman's rho	AI	Correlation coefficient	1.000	.050
		Sig. (2 tailed)	.	.818
		N	24	24
	Return to Sports	Correlation coefficient	.050	1.000
		Sig. (2 tailed)	.818	.
		N	24	24

**. Correlation is significant at the 0.05 level (2-tailed).

Discussion

Various regenerative cartilage surgeries have been reported to have wide variety of reported outcomes and success rate. Each has their advantage and disadvantages [3]. Innovative techniques to accomplish single stage procedures with the formation of durable repair tissue is the current leading-edge research [18]. Previous studies demonstrated that HA-BMAC-microfracture revealed better clinical outcomes in comparison to microfracture alone [6]. Many previous studies concluded that the coverage of cartilage defects with the scaffold implant was safe, feasible and in general improved the overall functional scores [10,11,19].

The data of this study revealed that the patients who underwent single stage cartilage repair technique via Hyaluronic- based scaffold implantation embedded with bone marrow derived cells combined microfracture procedure generally demonstrated successful short term and midterm functional outcome based on IKDC scores, Lysholm scores, patient abilities to perform the prayers and return to sports.

IKDC and Lysholm

Clinical outcome assessment with IKDC and Lysholm scoring showed significant improvement at short term (1 year and 2 years)

and midterm follow up (4 years) as compared to pre-operative status. Good outcomes were achieved across a wide range of patient's age, lesion sizes, compartment involved and associated injuries treated concurrently with cartilage repair. However, there was a decline in scoring from 1 year to 2 years of follow up and from 2 years to 4 years of follow up which was statistically significant. As the follow up years progressed the scores dropped. Due to cost and ethical issues, routine post-operative MRI, arthroscopy and biopsy was not done. Hence no objective measurements to assess the cartilage condition at each point of these follow up stages. The score drop can also be due to many other factors (not related to the surgery) as well that were not considered in this research. This includes the psychological component, and advancement in age with decline in activity level [11].

Return to sports

There were 9 patients who were playing sports at a competitive level and the remainder for leisure. All patients after their injury were never able to go back to their sports activities. However, some went back to sports after surgery but was never able to return to their pre-injury level of sports. There was statistically significant difference in the proportion of return to sports outcomes with relation to pre-operative scoring. However, the outcome between each interval did not elicit any difference. At final follow up 4 years, only 25% of the patients (6) went back to playing their desired sports but never to maximum capacity as they were at pre-injury. Out of the 6, 5 patients were from the competitive sports group. Age, lesion size, associated injuries and compartment involved did not have statistical effect on the clinical outcome of return to sports. Having said that, most of the patients who returned to sports were aged less than 40 years old, lesion size smaller than 4 cm^2 and with lateral compartment lesion. None of the patients with patellofemoral compartment lesion went back to sports. But in terms of presence of associated injuries, 67% return to sports were from the group with associated injuries.

Prayers

Performing our daily prayers in our culture needs repeated flexion and extension of the knees which includes deep flexion. We can conclude from this study that significant improvement in post-operative scores was noted. Comparative analysis of patients grouped by age below 40 years old or 40 years old and above, lesion size < 4 cm^2 and ≥ 4 cm^2 and presence of associated injuries did not demonstrate any significant differences in final outcome of prayers. We also noticed the comparative analysis with respect to compartment involved did have significant clinical outcome. All patients in the patellofemoral compartment group never returned to praying normally (kneeling on knees in deep flexion).

Age/Lesion size/Associated injuries

There was no statistical difference in outcome analysis patients below 40 years old and 40 years old and above at 4 years of post op follow up but the correlation analysis was negative suggesting that less successful outcome with increasing age. This can be due to the limitation of small sample size of our study. However, this treatment option should be considered in an indicated older patient. Size of the lesion (< 4 cm^2 and ≥ 4 cm^2) and associated injuries had no significant statistical significance in functional outcome at 4 years post op. This treatment option should be considered in indicated patients with wide range of lesion sizes and those with associated injuries which need intervention at the same setting.

Conclusion

Knee cartilage injury treatment using a hyaluronic acid–based scaffold with activated BMAC and microfracture provides good clinical outcomes at short and mid-term follow-up. However interesting finding in this study shows that although the objective scoring improved but none of the patients went back to pre-injury level sports, including those who were playing competitive sports. All patients in the patellofemoral compartment group never returned to praying normally.

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