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Original Article

Platelet rich plasma combined with arthroscopic microfracture versus arthroscopic microfracture alone for the treatment of knee cartilage injury

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Abstract: Objective: To investigate the clinical efficacy of platelet-rich plasma (PRP) injection combined with arthroscopic microfracture technique in treating knee cartilage injury. Methods: The clinical data of 120 patients with knee cartilage injuries treated in Jiangnan University Medical Center from October 2019 to December 2021 were analyzed retrospectively. Among them, 55 cases underwent the arthroscopic microfracture technique alone (control group), and the other 65 cases underwent PRP combined with the arthroscopic microfracture technique (observation group). The visual analogue scale (VAS) score, Lysholm knee joint score, MRI image indexes, the incidence of adverse events, and patient satisfaction during treatment were compared between groups before and after surgery. Results: Before surgery and at 3, 6, and 12 months after surgery, VAS scores in both groups showed a decreasing trend with time ($F = 40.780$, $P<0.001$); VAS scores in the observation group were lower than those in the control group ($F = 302.300$, $P<0.001$); there was an interaction between grouping and time ($F = 10.350$, $P<0.001$); Lysholm score in both groups showed an increasing trend with time ($F = 153.500$, $P<0.001$); Lysholm scores in the observation group were higher than those in the control group ($F = 488.000$, $P<0.001$); there was an interaction between grouping and time ($F = 25.570$, $P<0.001$). At 12 months after surgery, the subchondral bone marrow oedema volumes and bone marrow defect areas in the observation group were smaller than those in the control group; while repaired cartilage thicknesses of the observation group were more significant than those of the control group (all $P<0.05$). Patient satisfaction in the observation group was higher than that the control group (95.38% VS 80%, $P<0.05$). There was no statistical difference in the incidence of adverse events between the control group and the observation group (7.27% VS 3.64%). The clinical efficacy was judged to be effective in 81 cases and markedly effective in 39 patients. Logistic regression analysis showed that age and body mass index (BMI) were independent factors affecting the treatment efficacy. Conclusion: PRP combined with the arthroscopic microfracture technique has high safety in treating knee cartilage injuries. Compared with the arthroscopic microfracture alone, PRP combined with arthroscopic microfracture technique can effectively relieve pain, promote the repair of defective cartilage, improve knee joint function, and increase patient satisfaction. It is worthy of clinical promotion.

Keywords: Knee joint, cartilage injury, PRP, microfracture technique, arthroscope

Introduction

Articular cartilage is composed of chondrocytes and an extracellular matrix. It is a terminally differentiated tissue without blood vessels, nerves, or lymph, and its self-repair ability after the injury is poor. The knee joint is the most load-bearing joint in human body and is prone to cartilage injury. Clinical data show that cartilage injury accounts for 63% of knee surgery [1]. Trauma is the leading cause of knee joint injury, and the symptoms are mainly pain, swelling, and leg weakness. It can be accompanied by joint tenderness and limited movement, affecting knee function. If not treated promptly and effectively, it will result in cartilage degradation and subchondral exposure, which may lead to secondary osteoarthritis and aggravate knee joint damage. The arthroscopic microfracture technique is a traditional means of cartilage injury repair, with less trauma, simple operation, and low cost. However, the homogeneity and the quality of cartilage repair was not good [2]. So, it is of great significance to search for a suitable therapeutic method to repair cartilage. Platelet-rich plasma (PRP) is a plasma product with a high platelet content obtained from the peripheral blood by centrifugation. PRP is also rich in various growth factors, which are believed to stimulate subchondral mesenchymal stem cells to differentiate into chondrocytes [3]. In recent years, intra-articular injection of PRP has gradually become a new method to treat cartilage injuries. However, there is still some controversy about the effect of PRP combined with arthroscopic microfracture in treating knee joint injuries. This study investigated the clinical impact of PRP injection combined with arthroscopic microfracture technique in treating knee cartilage injury to provide a reference for clinical decision-making.

Subject and methods

Research subjects

Clinical data of patients with knee cartilage injury treated in Jiangnan University Medical Center from October 2019 to December 2021 were analyzed retrospectively. Inclusion criteria: (1) patients diagnosed with knee cartilage injury by clinical MRI, CT, or X-ray; (2) patients aged 18-65; (3) patients treated with arthroscopic microfracture technique or PRP combined with arthroscopic microfracture technique; (4) patients with complete clinical data. Exclusion criteria: (1) patients combined with injury of the meniscus, obvious joint deformity, or gout; (2) patients combined with major systemic organ diseases; (3) patients combined with diseases of the blood system and immune system; (4) patients with concurrent malignancy; (5) patients with previous leg joint fracture or surgical history. The Medical Ethics Committee at Jiangnan University Medical Center examined and approved this study.

Grouping methods

The patients were grouped according to the surgical method they received. The attending physician determined the treatment of patients. Patients who received the arthroscopic microfracture technique were included in the control group, and patients who received PRP combined with the arthroscopic microfracture technique were included in the observation group.

Treatment methods

The patients in control group received general or spinal anesthesia in the prone position. A transverse incision of about 0.5-0.8 cm was made on the left and right sides of the patellar ligament at 0.5 cm on the medial and lateral tibial plateau of the knee joint as an arthroscopic approach. Physiological saline was used to flush the joint cavities to remove suspended particulate matter and cartilage debris. Basket forceps were used to remove free bodies in the joint cavity. A planer knife and a low-temperature radiofrequency knife were used to trim synovium hyperplasia in the joint cavity. After adequate exposure of the damaged cartilage area, isolated unstable cartilage fragments were removed with a cartilage scraper, and regular cartilage edges were ground with a grinder. Individual cartilage vertebrae was perforated at the subchondral bone injury in the area of cartilage defect, with a 4 mm hole, a 3 mm hole spacing, and a 5 mm hole depth. Fat droplets or blood leakage from the holes was considered, and the joint cavity was aspirated to observe whether the damaged area was filled after the formation of a blood clot on the wound. Drill holes were added if necessary. Drainage film was placed, and routine postoperative rehabilitation was carried out. Follow-up was conducted 3, 6, and 12 months after therapy, and MRI was performed at the final follow-up.

The treatment of the arthroscopic microfracture technique in the observation group was the same as in the control group. Three days after surgery, 20 ml venous blood was drawn. The centrifugal operation was performed twice at 4°C, 2000 r/min. The concentration of platelets in PRP and venous blood was determined to ensure that the concentration in PRP prepared was more than four times that in venous blood. The patients were placed in a supine position, and the needle was inserted at the cross point between the upper margin of the patella and the space between the patella and knee joint. Three ml of PRP was injected into the joint cavity. Passive knee flexion and extension were given ten times after injection, and bandage with sterile dressing and ice were applied for 15 min. Injections were given once a week on three consecutive occasions.

Evaluation indicators

Main outcome measures: Visual analogue scale (VAS) [4] score was assessed before and 3, 6, and 12 months after the treatment. The VAS score ranges from 0-10 points. The higher the score, the more severe the pain. Lysholm knee score [5] was assessed before and 3, 6, and 12 months after the treatment. The score ranged from 0-100 points. The higher the score, the better the knee function. The curative effect was judged according to the VAS score and Lysholm knee score 12 months after the operation. Markedly effective: the Lysholm knee score >85 points, VAS score ≤3 points; effective: 65< the Lysholm knee score ≤85, VAS score ≤3; ineffective: the Lysholm knee score ≤65 points, VAS score >3 points.

Secondary measurement indicators: MRI examination results of fracture sites before and 12 months after surgery, including bone marrow oedema volume of subchondral bone, cartilage defect area, and repair cartilage thickness at the same position. The patient's satisfaction was measured after 14 days using our hospital's self-made satisfaction survey scale. The satisfaction scale consisted of 15 questions with a total score of 100 points, divided into four grades: unsatisfactory, satisfactory, relatively satisfactory and very satisfactory. The occurrence of adverse events during hospitalization, such as infection, hematoma, thrombosis, etc were recorded.

Statistical methods

SPSS23.0 was used for data processing. Quantitative data conforming to a normal distribution was described by mean ± standard deviation ($\bar{x} \pm s$). Paired sample t-test was used for comparison before and after the treatment. An independent sample t-test was used to compare between the two groups. Qualitative data were described by "n (%)", and the chi-square test or continuity correction test was used as appropriate. The VAS and Lysholm score of the two groups before and 3, 6, and 12 months after the operation were compared by repeated measurement analysis of variance and then corrected by the Bonferroni test. Patient satisfaction was compared using the rank sum test. The logistic regression analysis model was used to analyze the factors affecting the therapeutic effect of knee cartilage injury. $P<0.05$ was regarded as statistically significant.

Results

Research subject selection process

A total of 328 patients with knee cartilage injuries were identified between October 2019 and December 2021 by preliminarily searching the electronic information system of our hospital. A total of 78 cases were excluded due to age limits. Additionally, 94 patients were excluded due to not receiving treatment required for this study. Another 8 cases were transferred during treatment and thus were excluded. After preliminary screening, 28 cases with incomplete clinical data and surgical records were excluded. Finally, a total of 208 cases were excluded, and the other 120 cases were included (**Figure 1**). According to the different surgical methods, they were divided into a simple arthroscopic microfracture group (control group, n = 55) and PRP combined with arthroscopic microfracture group (observation group, n = 65).

Basic information

Table 1 shows the general data of two groups of patients.

VAS scores of both groups before and after treatment

VAS scores in the observation group were lower than those in the control group at 3, 6, and 12 months after surgery (intergroup effect: F = 302.300, $P<0.001$). VAS scores of both groups showed a decreasing trend over time (Time effect: F = 40.780, $P<0.001$). There was an interaction between grouping and time (F = 10.350, $P<0.001$, **Figure 2**).

Lysholm scores of both groups before and after treatment

Lysholm scores in the observation group were higher than those in the control group at 3, 6, and 12 months after surgery (intergroup effect: F = 488.000, $P<0.001$). Lysholm scores of both groups showed an increasing trend over time (Time effect: F = 153.500, $P<0.001$). The grouping interacted with time (F = 25.570, $P<0.001$, **Figure 3**).

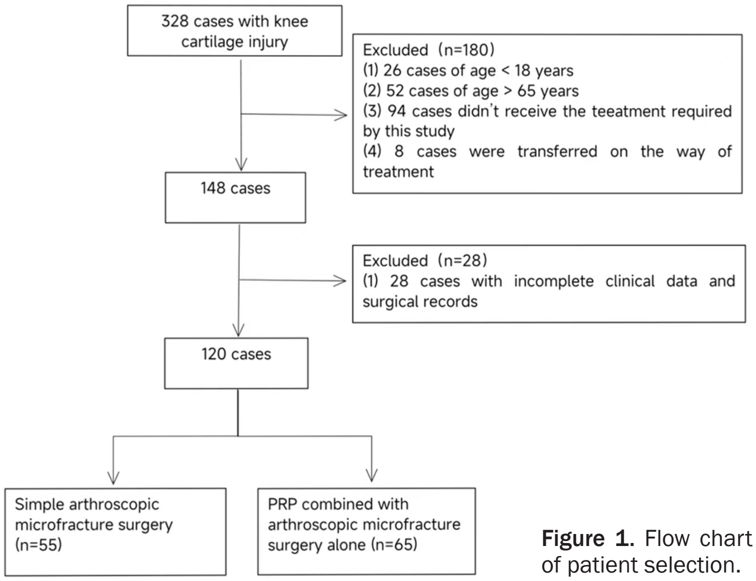

Figure 1. Flow chart of patient selection.

Table 1. Basic information of the two groups

Data	Control group (n = 55)	Observation group (n = 65)
Age		
<40 age	15 (27.27)	48 (73.85)
≥40 age	40 (72.73)	17 (26.15)
Sex		
male	31 (56.36)	38 (58.46)
female	24 (43.64)	27 (41.54)
BMI		
<24 kg/m^2	20 (36.36)	56 (86.15)
≥24 kg/m^2	35 (63.64)	9 (13.85)
Damage side		
left side	34 (61.82)	42 (64.62)
right side	21 (38.18)	23 (35.38)
Course of disease		
<22	15 (27.27)	42 (64.62)
≥22	40 (72.73)	23 (35.38)
Outer bridge grading		
I	4 (7.27)	6 (9.23)
II	8 (14.55)	10 (15.38)
III	26 (47.27)	30 (46.15)
IV	17 (30.91)	19 (29.24)
Combined underlying diseases		
hypertension	6 (10.91)	9 (13.85)
diabetes	14 (25.45)	11 (16.92)
coronary heart disease	5 (9.09)	3 (4.61)
Combined history of knee joint injury		
Yes	21 (38.18)	13 (20.00)
No	34 (61.82)	52 (80.00)

Note: BMI: body mass index. The Outer bridge is graded as an articular cartilage injury grading system. The higher the grade, the more severe the injury.

MRI image indexes before and after treatment of both groups

Twelve months after surgery, the subchondral bone marrow oedema volume and cartilage defect area of the observation group were significantly smaller than those of the control group, while the repaired cartilage thickness of the observation group was greater than those of the control group (all P<0.05, **Table 2**).

Incidence of adverse events during treatment of both groups

There was no statistical difference in the incidence of adverse events during treatment between the control and observation group (7.27% VS 3.64%, P>0.05, **Table 3**).

Patient satisfaction after treatment of both groups

Patient satisfaction in the observation group was better than those in the control group, and the difference was statistically significant (95.38% vs 80%, P<0.05, **Table 4**).

Analysis of the influencing factors of knee cartilage injury

After 12 months of treatment, the efficacy was effective in 81 cases and markedly effective in 39 cases. The results of the univariate analysis showed significant differences in age, BMI, course of disease and history of knee joint trauma between patients with practical clinical efficacy and patients with effective clinical efficacy (**Table 5**). Logistic regression analysis showed that age and BMI were independent factors affecting the treatment efficacy of knee cartilage injury, and age <40 years

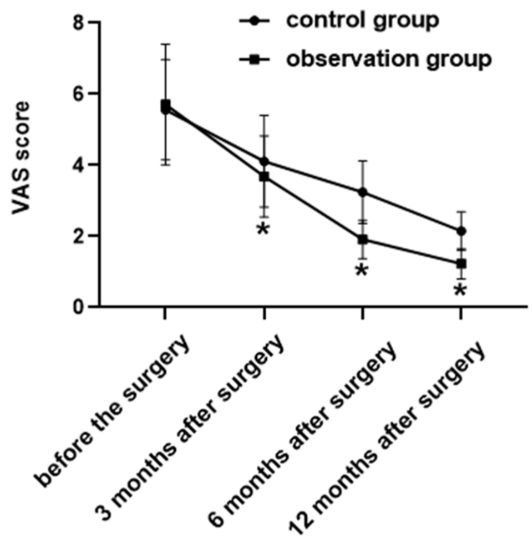

Figure 2. VAS score of the two groups. *, compared with the control group, $P<0.05$.

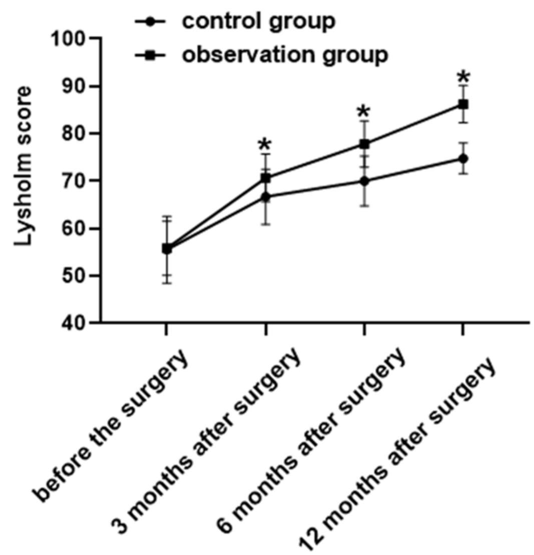

Figure 3. Lysholm scores of both groups. *, compared with the control group, $P<0.05$.

and BMI <24 kg/m^2 were protective factors (**Tables 6**, **7**).

Discussion

The treatment of knee cartilage injury has always been an essential problem in orthopedics. The arthroscopic microfracture technique is a minimally invasive treatment with high safety, which has been applied in clinical practice since the 1980s. The microfracture surgery first removes the diseased cartilage under arthroscopy, and then drills a small hole in the bone below the cartilage in the position where the cartilage is defective, so that a part of the bone marrow and blood seeps from the hole to form a blood clot, and then uses the stem cells in the blood to differentiate into chondrocytes to promote cartilage repair. It is one of the methods commonly used in clinical cartilage injury repair at this stage [6]. In an ideal state, the cure of cartilage lesions should achieve the healing of natural hyaline cartilage tissue, recovery of function and biomechanics and provide the integration of complete cartilage tissue. However, the cartilage produced by microfracture surgery is fibrous, which differs from natural hyaline cartilage in composition and properties. Fibrocartilage is made of type II collagen and has fewer chondrocytes. Therefore, its elasticity, stiffness, and wear resistance are worse than hyaluronic cartilage [7]. Despite differences from natural cartilage, microfracture surgery still shows good clinical results. However, the durability and applicability of regenerated cartilage after microfracture surgery is controversial. So, it is necessary to actively search for transparent cartilage tissue with higher stability that is helpful for rapid repair and formation of damaged sites to improve clinical efficacy and delay the progress of arthritis.

PRP is a plasma product isolated from autologous peripheral blood with a platelet content higher than average concentration. Activated platelets can release various high-concentration growth factors, such as insulin-like growth factor, primary fibroblast growth factor, and platelet-derived growth factor. These growth factors can promote the repair of cartilage defects, stimulate the proliferation of chondrocytes and mesenchymal stem cells, inhibit apoptosis of chondrocytes and mesenchymal stem cells, promote the synthesis of proteoglycan and collagen II in chondrocytes, and induces the differentiation of stem cells into chondrocytes [8-10]. At the same time, PRP contains fibrinogen and other coagulation factors, which can be activated to form temporary fibrin scaffolds for chondrocyte adhesion, migration, and proliferation. PRP can also reduce the catabolic effect of inflammatory factors such as interleukins on the cartilage [11]. This provides a good repair environment for knee cartilage

Table 2. MRI image indexes of the two groups

Grouping	Case	Subchondral bone marrow edema volume (cm^3)		Cartilage defect area (cm^2)		Thickness of repaired cartilage (mm)	
		Preoperative	12 months after surgery	Preoperative	12 months after surgery	Preoperative	12 months after surgery
Control group	55	1.06±0.31	0.41±0.12	2.27±0.73	1.85±0.47	2.41±0.61	1.83±0.33
Observation group	65	0.99±0.28	0.23±0.04	2.14±0.67	1.16±0.32	2.46±0.56	2.24±0.52
t		1.310	10.773	1.033	9.179	0.490	5.015
P		0.193	<0.001	0.304	<0.001	0.625	<0.001

Table 3. Incidence of adverse events in the two groups during treatment

Grouping	Case	Infection	Malunion of incision	Swelling	Total
Control group	55	2 (3.64)	2 (3.64)	0	4 (7.27)
Observation group	65	0	1 (1.54)	1 (1.54)	2 (3.64)
χ^2		3.161	0.541	1.233	0.397
P		0.075	0.462	0.267	0.528

Table 4. Patient satisfaction of the two groups

Grouping	Case	Not satisfied	Basically satisfied	Satisfied	Very satisfied	Total
Control group	55	11 (20.00)	22 (40.00)	15 (27.27)	7 (12.73)	44 (80.00)
Observation group	65	3 (4.62)	16 (24.62)	27 (41.54)	19 (29.23)	62 (95.38)
Z/χ^2		-3.598				5.431
P		<0.001				0.020

injury. Relevant studies [12] have shown that, adding PRP to cultured mesenchymal stem cells and chondrocytes *in vitro* can promote the integration of repaired cartilage and normal cartilage and promote cell proliferation and chondrogenesis of chondrocytes. PRP has excellent potential in the treatment of knee cartilage injuries.

The results of this study showed that the VAS scores of the two groups decreased gradually with time, and Lysholm scores increased with time. The VAS score of the observation group was significantly lower than that of the control group, and the Lysholm score was considerably higher than that of the control group. This suggests that arthroscopic microfracture combined with PRP can effectively improve short and medium-term pain and knee function after treatment of knee cartilage injury. After 12 months of surgery, bone marrow oedema volume and cartilage defect area of subchondral bone in the observation group were significantly smaller than those in the control group, and the repaired cartilage was markedly thicker than that in the control group, suggesting that arthroscopic microfracture combined with PRP can promote cartilage repair and improve the therapeutic effect. The above results are consistent with the results of Liang H et al. [13] that PRP can repair the local tissue of knee joint cartilage defects to improve patients' pain indirectly. Although PRP has no anti-inflammatory and analgesic components, it can regulate the synthesis of endogenous sodium hyaluronic [14]. Sodium hyaluronate lubricates the joint cavity to reduce friction. PRP can also inhibit the inflammatory response at the site of injury. In addition, the tissue repair time is longer, and with the gradual regression of the inflammatory response, the degree of pain in patients gradually decreases. The role of PRP in cartilage repair mainly lies in promoting synthesis and inducing cartilage regeneration. During cartilage repair, PRP stimulates damaged cartilage directly through platelet growth factors. These growth factors play an essential regulatory role in injured cartilage, and knee cartilage repair has a positive effect [15, 16]. The arthroscopic microfracture technique is a bone marrow stimulation technique that stimulates the differen-

Table 5. Single factor analysis of knee cartilage injury [n (%)]

Factor	Effective (n = 81)	Markedly effective (n = 39)	χ^2	*P*
Age			13.820	<0.001
<40 age	33 (40.74)	30 (76.92)		
≥40 age	48 (59.26)	9 (23.08)		
Sex			0.914	0.339
Male	49 (60.49)	20 (51.28)		
female	32 (39.51)	19 (48.72)		
BMI			11.269	0.001
<24 kg/m^2	43 (53.09)	33 (84.62)		
≥24 kg/m^2	38 (46.91)	6 (15.38)		
Course of disease			6.386	0.011
<22 month	32 (39.51)	25 (64.10)		
≥22 month	49 (60.49)	14 (35.90)		
Damage side			0.015	0.903
left side	51 (62.96)	25 (64.10)		
right side	30 (37.04)	14 (35.90)		
Outer bridge			2.217	0.145
I	9 (11.11)	1 (2.56)		
II	14 (17.28)	4 (10.26)		
III	34 (41.98)	22 (56.41)		
IV	24 (29.63)	12 (30.77)		
Combined underlying diseases			0.234	0.629
hypertension	11 (13.58)	4 (10.26)		
Diabetes	18 (22.22)	7 (17.95)		
Coronary	5 (6.17)	3 (7.69)		
Combined history of knee joint injury				
yes	53 (65.43)	33 (84.62)	4.771	0.029
no	28 (34.57)	6 (15.38)		

Note: BMI: body mass index.

Table 6. Assignments of influencing factors of curative effect of knee cartilage injury

Factor	Assignment
Age	<40 age = 0, ≥40 age = 1
BMI	<24 kg/m^2 = 0, ≥24 kg/m^2 = 1
Course of disease	<22 months = 0, ≥22 month = 1
Combined history of knee joint injury	No = 0, Yes = 1

Note: BMI: body mass index.

Table 7. Logistic regression analysis of the factors affecting efficacy of knee cartilage injury

Factor	*B*	*S.E*	*OR*	*P*	*OR (95% CI)*
Age	-1.310	0.479	7.469	0.006	0.270 (0.105-0.690)
BMI	-1.345	0.526	6.527	0.011	0.261 (0.093-0.731)
Course of disease	-0.591	0.457	1.674	0.196	0.554 (0.226-1.356)
history of knee joint injury	-0.848	0.548	2.399	0.121	0.428 (0.146-1.252)

Note: BMI: body mass index.

tiation of bone marrow mesenchymal stem cells to complete the repair of defective cartilage. PRP combined with the arthroscopic microfracture technique provides adequate mesenchymal stem cells as seeds for restoration and concentrated growth factors as nutrients. Theoretically, it can repair defective areas of cartilage to achieve a relatively good clinical effect. There was no statistical significance in the incidence of adverse events between groups during treatment. This suggests that PRP combined with arthroscopic microfracture technique has the same safety profile as the arthroscopic microfracture technique alone. This is coincident with the findings of Lin C et al. [17]. PRP has been widely used in treating orthopedic diseases and has become a vital non-surgical treatment. The regenerated cartilage after PRP treatment was close to normal cartilage histologically and biomechanically. Moreover, PRP is self-derived, without disease transmission and immune response, which dramatically increases the safety profile [18]. Patient satisfaction in the observation group was observably higher than in the control group. This may concern the practical improvement of pain and knee function by PRP combined with the arthroscopic microfracture technique. In this way, patients' postoperative experience is improved, thus gaining a favorable impression of patients. This study also showed that age <40 years and BMI <24 were protective factors for the treatment efficacy of knee cartilage injury. Therefore, patients aged over 40 or who are obese should be appropriately monitored after treatment. The sample size of this study is small, and it is a retrospective study, resulting in a particular bias in the results. At present, arthroscopy is the gold standard for cartilage repair. This study used MRI to review the cartilage repair after treatment in two groups. Although MRI examination is more popular and convenient in testing cartilage repair, it still has obvious limitations. High-quality prospective trials with larger sample size are also expected in the future. Arthroscopy also needs to be improved to provide detailed and accurate research data.

In conclusion, PRP combined with arthroscopic microfracture technique has high safety in treating knee cartilage injuries. Compared with the arthroscopic microfracture alone, PRP combined with the arthroscopic microfracture technique can effectively relieve pain, promote repair of defective cartilage, improve knee joint function, and increase patient satisfaction. Therefore, it is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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