Arthroscopic cartilage regeneration facilitating procedure

A decompressing arthroplasty for knee osteoarthritis

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Abstract

The effectiveness of arthroscopic treatment for knee osteoarthritis (OA) has always been a subject of debate. This study presents an innovative concept for the arthroscopic management of knee OA and investigates its clinical outcomes. An arthroscopic cartilage regeneration facilitating procedure (ACRFP) was performed on 693 knees of 411 patients with knee OA, with a mean age of 60 years (34–90 years), to eliminate the medial abrasion phenomenon (MAP) and decompress the patellofemoral joints. The Knee Society Score (KSS) and Knee Injury and Osteoarthritis Outcome Score (KOOS) were used to determine the subjective outcome. Roentgenographic changes in all cases and magnetic resonance imaging (MRI) variations in 20 randomly selected cases were evaluated for objective outcomes. We evaluated 634 knees in 369 patients (93.7%) with more than 3 years of follow-up (mean, 40 months; SD, 9) and found that the overall subjective satisfaction rate was 91.1%. Scores for KSS and all KOOS subscales improved statistically. Reversal of cartilage degeneration was observed in 80.1% of the entire series (radiographic outcome study) and 72.2% of the 18 randomly selected cases (1-year MRI outcome study). We found significant association between gender and OA severity, with regards to the subjective outcomes. Age, body mass index, pre-operative hyaluronic acid injection, OA severity, and type and severity of the medial plica were found to be important predictors of radiographic outcomes. An analysis of failed cases reaffirmed the need for early ACRFP and skilled post-operative care. ACRFP is an effective treatment for knee OA. It can benefit most patients and modify their degeneration processes if performed in time. However, further investigations are needed to confirm our concept of treatment.

Abbreviations: ACRFP = arthroscopic cartilage regeneration facilitating procedure, BMI = body mass index, FSE = fast spin echo, FTA = femorotibial angle, HA = hyaluronic acid, JSW = joint space width, KOOS = knee injury and osteoarthritis outcome score, KSS = knee society score, MAP = medial abrasion phenomenon, MRI = magnetic resonance imaging, NEX = number of excitations, OA = osteoarthritis, TR/TE = repetition time/echo time, WORMS = whole-organ MRI score.

Keywords: arthroplasty, arthroscopy, cartilage, medial abrasion phenomenon, medial plica, osteoarthritis, regeneration.

1. Introduction

Knee osteoarthritis (OA) remains an alarming public health concern worldwide in terms of health-related quality of life and the financial burden of the disease. Currently, it is regarded as incurable, and no approved medication or surgical procedure (e.g., arthroscopic debridement, microfracture, chondrocyte transplantation, osteotomy) can halt progressive destruction of the osteoarthritic knee joint. Conventional treatment provides only symptomatic relief rather than preventative or regenerative results and may eventually lead to total knee arthroplasty (TKA).

Since 2006, several studies have investigated the medial abrasion phenomenon (MAP) as a cause of knee OA. Medial plica-related MAP has been found to have a close relationship with knee OA. MAP elicits a lifelong interplay between a pathologic medial plica and the facing medial femoral condyle, playing a vital role in the pathogenesis of knee OA through both physical and chemical effects. Consequently, arthroscopic medial release (AMR) and arthroscopic cartilage regeneration facilitating procedure (ACRFP) have been developed to treat knee OA. The outcome of these studies and the subsequent positive feedback from the clinical applications of this concept, called the knee health promotion option for the comprehensive treatment of knee OA, persuaded us to standardize this technique further and scrutinize its clinical outcomes. We believe this to be an excellent example to showcase the importance of translational medicine. We propose that the ACRFP offers the...
following benefits: eradication of damaging factors and decompression of the knee joint, which should be maintained by meticulous post-operative care to provide the damaged cartilage an opportunity for regeneration.

2. Methods

2.1. Patients

In 2013, 548 patients (924 knees) with knee OA received surgical treatment at our institution. Patients with OA of any stage treated conservatively for more than 6 months without improvement were included. Patients were excluded if they had instability due to a previous ligament injury or OA due to fracture malunion. The treatment options for individual patients were decided according to our clinical staging system (Table 1) and treatment guidelines (Table 2). The stage of the knee OA is determined by the most advanced stage of the 2 weight-bearing compartments. Eventually, 411 patients (693 knees) who had received ACRFP were prospectively followed up as part of an institutional review board registry. There were 99 (24.4%) men and 312 (75.6%) women with a mean age of 60 years (34–90 years) at the time of the surgery. The medial compartment was primarily involved in 638 knees (92.1%) of 363 patients, and the lateral compartment in 55 knees (7.9%) of 48 patients. The duration of symptoms, surgical history, glucosamine sulfate intake, or administration of hyaluronic acid (HA) injections for more than 1 year were recorded. Twenty bilateral Stage III female patients (40 knees) older than 60 years were randomly recruited to voluntarily join the magnetic resonance imaging (MRI) study. All the methods and procedures were performed following the relevant guidelines and regulations of the Research Ethics Committee of our institution. Written informed consent was obtained from all participants.

2.2. Image protocol

The radiographic protocols to assess the tibiofemoral and patellofemoral joint spaces by standing extended anteroposterior and Merchant’s views as described in a previous study[12]

| Table 1 | Clinical staging for OA of individual knee compartments based on rentgenographic and clinical findings. |
|---------|----------------------------------------------------------------------------------------------------------|
| Stage   | Rentgenographic findings                           | Clinical findings |
| I       | Doubtful                                           | No               | Normal | Stable |
| II      | Definite, no more than 1/2                         | Doubtful         | <5°    | Stable |
| III     | Marked, more than 1/2                              | Deinite          | 5–10°  | Stable |
| IV      | Completely obliterated                            | Marked           | >10°   | Stable |
| V       | Completely obliterated                            | Marked           | >10°   | Unstable |

OA = osteoarthritis.

| Table 2 | Surgical treatment guideline for knee OA. |
|---------|------------------------------------------|
| Stage   | ACRFP | Osteotomy | UKA | TKA |
| I       | -     | -         | -   | -   |
| II      | +++   | -         | -   | -   |
| III     | ++++  | +         | ++  | -   |
| IV      | ++    | +         | +++ | ++  |
| V       | -     | +         | +++ | +++ |

ACRFP = arthroscopic cartilage regeneration facilitating procedure, OA = osteoarthritis, UKA = unicompartmental knee arthroplasty, TKA = total knee arthroplasty.

2.3. Surgical procedure

An arthroscopic examination was performed through the inferolateral portal. The presence of medial plica-related MAP and its sequelae (Fig. 1) was first investigated. The type and grading of the medial plica and that of 2 distinct foci of the cartilaginous lesions on the edge (focus A) and anterior part (focus B) of the medial femoral condyle, related to the impingement or abrasion caused by the medial plica during knee motion, as described in a previous study, were recorded.[13] The degree of cartilage degradation in each compartment was verified using the Outerbridge classification.[14]

Whether the menisci were torn or not was also noted.

The medial release was performed as described in previous studies.[11,12] After eradicating the inflammatory synovium and medial plica occupying the space over the intermedial region of the patella and medial gutter, the tight and obliterated medial facet of the patellofemoral joint was released by cautiously severing the medial retinaculum. The adequacy of the release was checked by passing the tip of the scope under the patella and verifying if the previously tight medial patellofemoral joint space (Fig. 2a) could be easily passed through, and the medial retinaculum was visualized (Fig. 2b). After medial release, the patella always deviated laterally (Fig. 2c). Taking advantage of the sharp dissection, the lateral release was performed by inserting a No. 11 scalpel into the inferolateral portal and percutaneously cutting the lateral retinaculum. The extent and adequacy of the release was evaluated by direct vision using an arthroscope (Fig. 2d).

Any focal synovitis or loose chondral flaps on the cartilaginous surface were removed as per conventional arthroscopic débridement for knee OA. No bony procedures such as drilling or micro fracture were performed.

2.4. Post-operative management

From the day of surgery, full range of motion, full weight-bearing, and free ambulation were allowed as tolerated. To reduce the likelihood of hemarthrosis, a suction drain was used for 24-48 hours. The patient was discharged 2 days postoperatively. Home exercise programs, including quadriceps strengthening and passive range of motion, were emphasized. Case managers strictly monitored patients’ adherence to the home exercise. No supplementary treatment, including oral glucosamine sulfate or intra-articular injection of HA or PRP, was administered throughout the post-operative period.

2.5. Follow-up and evaluation of clinical outcome

Patients returned for monthly evaluation 3 months postoperatively. Thereafter, they were examined during annual follow-up
visits. Both pre- and post-operative KSS and Knee Injury and Osteoarthritis Outcome Score (KOOS) were compared for subjective outcome evaluation. Patients were interviewed about their satisfaction with ACRFP using a categorical scale prepared for our study: excellent (free of symptoms, no limitation in activities), good (greatly improved, occasional pain, normal activities), fair (same as pre-operative condition, no improvement), and poor (received or considered further operative treatment). The outcome was considered satisfactory if the subjective satisfaction was “excellent” or “good.” All investigations focused on individual knees in bilateral cases.

2.6. Evaluation of image outcome

The pre-operative standing extended anteroposterior and Merchant’s radiographic views were compared with those taken at the last clinic follow-up on a picture archiving communication system workstation (INFINITT Healthcare Co., Ltd.). The interpretation parameters included the femoral-tibial angle (FTA), minimum joint space width (JSW), and surface contour of the joint lines. The interpretation resulted in the inference that the knee was better, the same, or worse following the ACRFP operation.

Baseline and follow-up MR images of the knees were transferred to a picture archiving communication system workstation and reviewed. The presence and grade of cartilage, meniscal, and bone marrow lesions (bone marrow edema and cysts) were assessed using a modified whole-organ MRI score (WORMS). The sum and maximum scores (WORMS Sum and WORMS max) were recorded for each category, and the difference in scores between the baseline and follow-up images (Δ WORMS Sum) were calculated.

Figure 1. Medial abrasion phenomenon and its sequelae. (a) pathologic medial plica (*) and lesion “A” (arrows) on the medial femoral condyle caused by focal abrasion; (b) lesion “B” (arrows) on the medial femoral condyle caused by synovitis on the medial plica (*); (c) impingement of medial plica (*) and tightness of patellofemoral joint due to chronic inflammation; (d) focal synovitis (*) over the inferomedial region of the patella.

Figure 2. The decompressing effects of ACRFP. (a) tight medial patellofemoral joint before medial release; (b) after adequate medial release, the previously tight medial patellofemoral joint space was opened, and the medial retinaculum (MR) was visualized; (c) after medial release, the patella would always deviate laterally; (d) after percutaneous lateral release, the lateral patellofemoral joint was wide open. ACRFP = arthroscopic cartilage regeneration facilitating procedure.
Two radiologists (LCW with 15 years and CYR with 6 years in musculoskeletal imaging) independently analyzed all radiographic and MR images. In any mismatched cases, a consensus was reached by co-reading.

2.7. Statistical analysis

Statistical analyses were performed using JMP (version 5.0.1.2, SAS Institute Inc., Cary, NC). All values are presented as the mean and standard deviation. A 1-way analysis of variance to detect differences in the distribution of patient age in each stage of OA was used to make comparisons. Analyses comparing pre-operative and post-operative KSS, KOOS, FTA, and JSW were performed using the paired t-test. A 2-sided P value (P < .05) was considered statistically significant. Logistic regression was used to analyze the response of subjective and radiographic outcomes as a function of age, BMI, symptom duration, pre-operative femorotibial angle, and JSW. Pearson’s chi-square or Fisher’s exact test was used to analyze the response of subjective and radiographic outcomes as a function of categorical variables (gender, glucosamine sulfate intake, HA injection, previous operation, meniscus tear, pre-operative staging, type and severity of medial plica, and grading of cartilage damage over hidden lesions and each compartment).

3. Results

There were 634 knees in 369 patients available for a thorough outcome study, including X-ray examinations, KSS, and KOOS evaluations. Sixteen of 196 knees (8.2%) with Stage II OA in 9 patients, 26 of 414 knees (6.3%) with Stage III OA in 17 patients, and 2 of 83 knees (2.4%) with Stage IV OA in 2 patients did not return for follow-up. The total follow-up rate was 93.7%, and the mean follow-up period was 40 months (SD, 9). The mean age and distribution of the different OA stages stratified by the main involved compartment are shown in Table 3. Patients with Stage II OA were younger than those with Stages III or IV OA. The medial compartment was primarily involved in 611 knees (94.1%) of the 357 patients, and the lateral compartment in 38 knees (5.9%) of the 26 patients. Eighteen patients (90%) with 36 knees of the 20 randomly recruited patients returned for the 1-year follow-up MRI evaluation.

The subjective outcome assessment (Table 4) was satisfactory in 391 knees (91.1%). Patients with Stage II disease had a higher satisfaction rate (P < .01). The Knee Society scores and all subscales of the KOOS were statistically improved in both the medial and lateral compartment groups (Tables 5 and 6). The FTA improved from 0.43 (SD 4.33) to 0.59 (SD 4.45) (P = .04) in the medial compartment group and did not show a statistical difference in the lateral compartment group (9.39/SD 4.10 to 9.66/SD 4.48; P = .51). The JSW increased from 2.73 (SD 1.34) to 2.98 (SD 1.43) (P < .01) in the medial compartment group and from 3.19 (SD 1.09) to 3.66 (SD 1.19) (P < .01) in the lateral compartment group. The radiographic outcome revealed an overall reversal of the degeneration process in 80.1% of the entire series (Table 7). For the whole series and the medial compartment group, the rate of reversal of the degeneration process was higher in the Stage II knees (P < .01). There was no statistical difference in the rate of reversal of the degeneration process between the medial compartment.

### Table 3

| Stage | Medial compartment (Age (SD)/No.) | Lateral compartment (Age (SD)/No.) | Total (Age (SD)/No.) |
|-------|----------------------------------|----------------------------------|---------------------|
| II    | 64* (10/178)                    | 61* (11/2)                      | 64* (10/180)        |
| III   | 70 (9/355)                      | 68 (8/33)                       | 70 (9/388)          |
| IV    | 70 (9/78)                       | 71 (17/3)                       | 70 (9/81)           |
| Total | 68 (10/611)                     | 68 (9/38)                      | 60 (10/649)         |

OA = osteoarthritis.

* Statistically significant compared to that of stage III and IV by comparisons for each pair using paired t test (P < .05).

### Table 4

| Stage | Medial compartment (N = 611) | Lateral compartment (N = 38) |
|-------|------------------------------|-----------------------------|
|       | E† G F P Sat. (%)            | E G F P Sat. (%)            | Total (%)            |
| II    | 74.2 (132) Romania           | 23.0 (41) Romania            | 2.8 (6)              | 0         | 97.2 | 50.0 (1) | 0 | 50.0 (1) | 0 | 50.0 | 96.7* |
| III   | 56.3 (200)                   | 32.1 (114)                   | 5.1 (18)             | 6.5 (23)             | 88.4 | 57.6 (19) | 30.3 (10) | 9.1 (3) | 3.0 (1) | 87.9 | 88.4 |
| IV    | 47.4 (37)                    | 43.6 (34)                    | 1.3 (1)              | 7.7 (6)              | 91.0 | 33.3 (1) | 66.7 (2) | 0 | 0 | 100.0 | 91.4 |
| Total | 60.4 (369)                   | 30.9 (189)                   | 3.9 (24)             | 4.8 (29)             | 91.0 | 55.3 (21) | 31.6 (12) | 10.5 (4) | 2.6 (1) | 86.9 | 91.1 |

OA = osteoarthritis.

† E: excellent; G: good; F: fair; P: poor; Sat.: satisfied = E + G, presented as % (N).

* Statistically significant by comparisons for each pair using paired t test (P < .05).

### Table 5

| Stage | Medial compartment (N = 105) | Lateral compartment (N = 29) |
|-------|------------------------------|-----------------------------|
|       | Pain (SD) Function (SD)      | Pain (SD) Function (SD)      |
|       | Pre-op. Post-op. Pre-op. Post-op. Pre-op. Post-op. Pre-op. Post-op. Pre-op. Post-op. Pre-op. Post-op. |
| II    | 68.8 (13.0) 89.8 (9.8) 58.6 (16.1) 86.2 (14.3) 74.5 (20.5) 87.5 (10.6) 40.0 (28.3) 55.0 (21.2) |
| III   | 65.8 (12.9) 86.0 (11.0) 53.5 (16.7) 79.2 (17.1) 65.9 (13.0) 84.6 (10.5) 57.7 (16.1) 74.5 (18.0) |
| IV    | 62.4 (14.6) 80.5 (15.0) 47.3 (16.9) 74.8 (17.4) 68.0 (6.1) 80.3 (9.5) 40.0 (20.3) 60.0 (40.0) |
| Total | 66.3 (13.1) 86.4 (11.7) 54.2 (16.9) 80.7 (16.8) 66.5 (12.7) 84.4 (10.3) 55.4 (17.5) 72.4 (20.3) |

P value <.01

OA = osteoarthritis.
(80.0%) and lateral compartment groups (89.5%) (P = .11). MRI outcomes (Table 8) showed reversal of the degeneration process in 72.2% of cartilage, 63.9% of bone marrow edema, 63.9% of bone cyst, and 91.7% of meniscus categories of WORMS.

The analyses of factors influencing subjective and radiographic outcomes showed that gender, OA severity (JSW, FTA, X-ray staging, and arthroscopic grading of cartilage damage) are related to subjective outcomes. Age, BMI, pre-operative HA injection, OA severity (FTA, X-ray staging, and arthroscopic grading of cartilage damage), and the type and severity of the meniscal plica were found to be significantly related to radiographic outcomes (Table 9). Thirty knees (4.6%) in the whole series; 24 knees (6.2%) in the Stage III group and 6 knees (7.4%) in the Stage IV group; 29 knees (4.7%) in the medial compartment group, and 1 knee (2.6%) in the lateral compartment group deteriorated and eventually underwent arthroplasty. The relevant data for these failed cases are presented in Table 10. Twenty-four cases (80%) were arthroscopic grade IV with submeniscus erosion of the tibial plateau and, therefore, meniscus protrusion. Fifteen patients (50%) had low compliance with our post-operative self-rehabilitation protocol. Six of these patients had earlier arthroscopic grades (II and III) of the main involved compartment and no meniscus protrusion. All the failed cases with good compliance were arthroscopic grade IV with meniscus protrusion. All the low compliance cases received TKA in contrast to 53.3% of the cases with good compliance (the other 46.7% received unicompartmental knee arthroplasty). The average elapsed time between ACRFP and arthroplasty was 1.1 years for the group with low compliance as compared to 2.6 years for the group with good compliance.

The radiographic images showed indirect evidence of cartilage regeneration (Figs. 3 and 4). Furthermore, MRI studies also disclosed the possibility of cartilage regeneration (Fig. 5).

Table 6
Pre-operative and post-operative KOOS of different stage of OA stratified by main involved compartment.

| Stage (Number) | P (SD) | S (SD) | ADL (SD) | S/R (SD) | QOL (SD) |
|----------------|--------|--------|----------|----------|----------|
| Pre-op.        | Post-op. | Pre-op. | Post-op. | Pre-op. | Post-op. | Pre-op. | Post-op. | Pre-op. | Post-op. |
| Med. (178)      | 66.8 (17.0) | 88.4 (14.0) | 52.9 (15.2) | 84.2 (14.0) | 71.1 (19.0) | 91.5 (11.7) | 40.6 (26.4) | 68.2 (27.4) | 43.4 (20.1) | 70.2 (22.6) |
| Lat. (2)        | 58.5 (7.8) | 90.3 (13.7) | 32.0 (15.6) | 78.6 (10.1) | 67.5 (21.1) | 81.6 (3.1) | 27.5 (17.7) | 47.3 (10.6) | 47.0 (4.2) | 58.3 (11.3) |
| Med. (355)      | 63.1 (16.1) | 86.0 (15.0) | 52.9 (15.8) | 81.1 (16.2) | 68.1 (16.6) | 86.6 (15.2) | 30.1 (20.4) | 55.4 (32.2) | 38.7 (17.4) | 66.4 (25.1) |
| Lat. (33)       | 59.8 (18.1) | 83.2 (12.6) | 45.6 (19.1) | 73.8 (15.0) | 63.3 (22.9) | 83.9 (11.8) | 29.5 (26.0) | 44.1 (33.4) | 36.1 (19.4) | 61.0 (22.7) |
| Med. (76)       | 62.0 (17.7) | 84.3 (16.5) | 51.9 (14.8) | 78.2 (18.5) | 66.1 (18.1) | 85.3 (15.5) | 27.7 (21.7) | 49.6 (31.5) | 39.5 (20.0) | 63.3 (27.4) |
| Lat. (3)        | 60.3 (5.9) | 77.0 (20.6) | 46.3 (12.9) | 66.6 (13.1) | 57.7 (21.6) | 75.4 (21.5) | 20.0 (13.2) | 45.0 (26.5) | 37.7 (11.0) | 62.5 (37.5) |
| Total Med. (611)| 64.1 (16.7) | 86.5 (14.9) | 52.8 (15.5) | 81.6 (16.0) | 68.7 (17.6) | 87.9 (14.5) | 32.8 (23.0) | 58.4 (31.5) | 40.2 (18.6) | 67.1 (24.8) |
| Lat. (38)       | 59.8 (17.0) | 83.1 (13.1) | 44.9 (18.5) | 73.5 (16.0) | 63.1 (21.9) | 83.1 (12.3) | 28.7 (24.7) | 42.2 (38.8) | 38.6 (18.3) | 60.4 (23.2) |

P value <.01 <.01 <.01 <.01 <.01

KOOS = knee injury and osteoarthritis outcome score, OA = osteoarthritis.

Table 7
Radiographic outcome of different stage of OA stratified by main involved compartment.

| Stage | Medial compartment (N = 611) | Lateral compartment (N = 38) | Total (N = 649) |
|-------|-----------------------------|-----------------------------|----------------|
| Better | Same | Worse | Rev. DP | Better | Same | Worse | Rev. DP | Rev. DP |
| II | 65.2 (116) | 24.2 (43) | 10.6 (19) | 89.4 * (159) | 50.0 (1) | 50.0 (1) | 0 | 100 (2) | 89.4 * (161) |
| III | 59.8 (208) | 17.8 (63) | 23.6 (84) | 78.4 (271) | 66.7 (22) | 21.2 (7) | 12.1 (4) | 87.9 (29) | 77.3 (269) |
| IV | 52.6 (41) | 23.1 (18) | 24.3 (19) | 75.7 (60) | 66.7 (2) | 33.3 (1) | 0 | 100 (3) | 76.5 (62) |
| Total | 59.7 (365) | 20.3 (124) | 20.0 (122) | 80.0 (489) | 65.8 (25) | 23.7 (9) | 10.5 (4) | 89.5 (34) | 80.1 (523) |

OA = osteoarthritis.

† Reversed degeneration process (Rev. DP) = Better + Same, presented as % (N).

* Statistically significant by comparisons for each pair using paired t test (P < .05).

4. Discussion
This report presents the surgical procedure, the standard post-operative self-rehabilitation protocol, and clinical and imaging outcomes of ACRFP for knee OA. The overall subjective satisfaction rate was 91.1% after at least 3 years of follow-up. The KSS and KOOS surveys showed improvements in clinical symptoms and quality of life. Radiographic evaluations and comparisons showed that the degeneration process was reversed in 80.1% of the knees after ACRFP. The 1-year MRI outcome study also demonstrated reversal of the cartilage degeneration in 72.2% of the randomly selected Stage III cases.

The subjective satisfaction rate here was better than that in previous report.[12] This might be the consequence of technique improvement by standardizing the surgical procedure and meticulous post-operative self-rehabilitation programs. Analyses of the factors influencing outcomes revealed that gender and OA severity were related to subjective outcomes. Age, BMI, pre-operative HA injection, OA severity, and type and severity of the medial plica were important predictors of radiographic outcomes. The negative correlation of age, BMI, and OA severity with outcomes emphasizes the importance of early ACRFP intervention. Better subjective outcomes in women may be attributed to their hypersensitivity to pain.[19] Worse radiographic outcomes in patients receiving pre-operative HA injections may be explained by the reactive arthrofibrosis or infrapatellar fat pad fibrosis, which is a common arthroscopic finding in patients who have received multiple injections or experienced failed extra-articular injections. The masking effect of HA injections might also have delayed ACRFP intervention. The analysis of failed cases reconfirmed that early intervention and meticulous post-operative care both contribute to successful ACRFP. Patients with low compliance with our self-rehabilitation protocol, thus developing arthrofibrosis, are more likely to undergo earlier or even unnecessary TKA.
Although articular hyaline cartilage was classically considered to have no or low potential for regeneration,\(^{[19]}\) some authors have reported both direct and indirect evidence of articular cartilage regeneration after correction of varus deformity for knee OA.\(^{[20,21]}\) Previous reports on AMR and ACRFP also demonstrated that on removing all existing catabolic factors, anabolism of the damaged cartilage may become dominant, and regeneration may ensue.\(^{[11,12]}\) The radiographic observation of the reversal of the degeneration process in 80.1% of the knees here coincides with the findings of a previous report of 81.2%.\(^{[12]}\)

Mechanical stresses play an important role in articular cartilage degradation.\(^{[22]}\) It has been shown that static compression suppresses matrix biosynthesis, whereas cyclic and intermittent loading can either stimulate or suppress matrix synthesis, depending on the frequency or magnitude of loading. High rates or magnitudes of stress can induce an “injurious” response associated with increased degradation, cell death, and the production of matrix metalloproteinases.\(^{[23]}\) Technologies such as wedge insoles, unloading knee brace, high tibial osteotomy, and knee joint distraction that “unload” the joint may reverse the structural damage.\(^{[24,25]}\) Regarding the anabolic effects of ACRFP, in addition to the elimination of the physical abrasion damage of MAP and the chemical erosion of focal inflammatory tissues, another critical factor is the release of increased static pressure in the patellofemoral joint, which is caused by lifelong, repeated inflammation induced by MAP. These anabolic effects obtained by the ACRFP provide favorable conditions for cartilage regeneration in the medial compartment and benefit the lateral and patellofemoral compartments, as proven by this study and a previous report.\(^{[12]}\) A recent gait analysis study also observed the effect of the modification of dynamic foot pressure and gait pattern after ACRFP, which are beneficial to the cartilage.\(^{[26]}\)

### Table 8

| MRI outcomes stratified by main categories of WORMS. | Cartilage | Bone marrow edema | Bone cyst | Meniscus |
|---------------------------------------------------|-----------|-------------------|-----------|----------|
| Get worse                                         | 27.8 (10) | 36.1 (13)         | 36.1 (13) | 8.3 (3)  |
| Same                                              | 38.9 (14) | 41.7 (15)         | 58.3 (21) | 91.7 (33)|
| Improved                                          | 33.3 (12) | 22.2 (8)          | 5.6 (2)   | 0 (0)    |
| †Rev. DP                                          | 72.2 (26) | 63.9 (23)         | 63.9 (23) | 91.7 (33)|

MRI = magnetic resonance imaging, WORMS = whole-organ MRI score.
† Reversed degeneration process (Rev. DP) = Better + Same, presented as % (N)

### Table 9

| Analyses of factors influencing subjective and radiographic outcomes. |
|---------------------------------------------------------------|
| Subjective outcome (Satisfied or not) | Radiographic outcome (RDP or not) |
| Med. comp. (N = 611) | Lat. comp. (N = 38) | Med. comp. (N = 611) | Lat. comp. (N = 38) |

2 × 2 Contingency analyses
Data are presented as \(P\) values and odds ratios (95% confidence interval)

| Gender as female | .01* | .84 | .32 | .95 |
| Glucosamine intake | .64 | .78 (0.08-8.04) | .48 | 1.08 (0.10-11.92) |
| HA injection | 1.05 (0.13-8.38) | 0.39 (0.05-3.08) | 11.05 (0.54-223.91) |
| Previous operation | .41 | .64 | <.01* | 15 |
| Medial meniscus tear | 0.05 (0.25-1.51) | 0.38 (0.04-3.69) | 1.00 |
| Lateral meniscus tear | 0.41 | - | .59 | - |
| Medial plica | 1.84 (0.52-6.47) | 0.66 (0.19-2.28) | 1.00 |

Logistic regression analyses
Data are presented as \(P\) values

| Age | .17 | .67 | .04* | .62 |
| BMI | .21 | .58 | <0.01* | .05 |
| Duration of symptom | .53 | .10 | .32 | .24 |
| Pre-op. FTA | <0.01* | .72 | <0.01* | .40 |
| Pre-op. JSW | <0.01* | .28 | <0.01* | .95 |

Pearson’s chi-square test
Data are presented as \(P\) values

| X-ray staging | Medi | .67 | <0.01* | .66 |
| Lateral | .98 | .32 | .73 | .24 |
| PF | .84 | - | .73 | <0.01* |
| Medial plica | .75 | .73 | <0.01* | .95 |
| Type | .62 | .71 | .10 | <0.01* |
| Severity | - | .22 | .07 | .84 |
| Hidden lesion | .43 | .34 | .06 | .65 |
| Focus A | <0.01* | .22 | .07 | .84 |
| Focus B | - | .65 | .06 | .65 |
| Arthroscopic grading | MFC | .62 | <0.01* | .45 |
| MTP | <0.01* | .89 | <0.01* | .63 |
| LC | .21 | <0.01* | .14 | .14 |
| PF joint | .04* | .15 | .04* | .70 |

FTA = femorotibial angle, JSW = joint space width, LC = Lateral compartment, MFC = medial femoral condyle, MTP = medial tibial plateau, PF = patellofemoral, RDP = reversed degeneration process.
* Denotes statistical significance.
including lavage, debridement, abrasion arthroplasty, microfracture, and autologous chondrocyte implantation for knee OA,[1,27–30] ACRFP has a more precise rationale for treatment and can obtain more reproducible and beneficial outcomes. The outcome of this study affirms that in addition to eradicating the MAP, the key to a successful ACRFP is to adequately release the tightness of the patellofemoral joint and maintain this appropriate tension around the patella by a skillfully supervised post-operative self-rehabilitation regimen to prevent recurrent tightness that may develop from scarring and arthrofibrosis.

However, this study had some limitations. First, our radiographic protocol for standing extended anteroposterior radiographs of the knee might cause some bias because the improvement in the ability to extend the knee after ACRFP might have brought about an apparent improvement in cartilage width. Second, properly conducted randomized controlled clinical trials and massive long-term MRI evaluations are needed to obtain more convincing evidence.

5. Conclusion
The imaging evidence of cartilage regeneration after ACRFP in this study substantiated the hypothesis that MAP is an important factor in the pathogenesis of knee OA. Moreover, if performed

Table 10

| No. | Pre-op. stage | Main comp. | FTA (mm) | JSW (mm) | Arthroscopic grading of main comp. | Meniscus protrusion | Low compliance in following post-op. protocol | Type of arthroplasty | Years after ACRFP when failed |
|-----|---------------|------------|----------|----------|----------------------------------|--------------------|-----------------------------------------------|--------------------|-------------------------------|
| 1   | IV            | M          | -6       | 1.10     | IV                               | Y                  | N                                             | UKA                | 3                             |
| 2   | III           | M          | -2       | 2.62     | IV                               | Y                  | N                                             | TKA                | 4                             |
| 3*  | IV            | M          | -3       | 3.35     | III                              | N                  | Y                                             | TKA                | 1                             |
| 4   | IV            | M          | -10      | 2.76     | IV                               | Y                  | N                                             | TKA                | 1                             |
| 5   | IV            | M          | -2       | 1.12     | IV                               | Y                  | N                                             | UKA                | 4                             |
| 6*  | III           | M          | -4       | 2.36     | IV                               | N                  | Y                                             | TKA                | 2                             |
| 7   | III           | M          | -5       | 1.01     | IV                               | Y                  | N                                             | UKA                | 3                             |
| 8   | III           | L          | 8        | 1.22     | IV                               | Y                  | N                                             | UKA                | 3                             |
| 9   | III           | M          | -2       | 1.35     | IV                               | Y                  | N                                             | TKA                | 1                             |
| 10  | III           | M          | -1       | 2.59     | IV                               | Y                  | N                                             | UKA                | 2                             |
| 11  | III           | M          | 0        | 1.92     | IV                               | Y                  | N                                             | UKA                | 2                             |
| 12  | III           | M          | -3       | 2.40     | IV                               | Y                  | N                                             | UKA                | 1                             |
| 13  | III           | M          | -5       | 1.12     | IV                               | Y                  | Y                                             | TKA                | 1                             |
| 14  | IV            | M          | -10      | 0.00     | IV                               | Y                  | Y                                             | TKA                | 1                             |
| 15  | IV            | M          | -11      | 0.00     | IV                               | Y                  | N                                             | TKA                | 3                             |
| 16  | III           | M          | -3       | 2.20     | IV                               | Y                  | Y                                             | TKA                | 1                             |
| 17  | III           | M          | -3       | 2.46     | IV                               | Y                  | Y                                             | TKA                | 1                             |
| 18  | IV            | M          | -5       | 0.86     | IV                               | Y                  | Y                                             | TKA                | 1                             |
| 19  | IV            | M          | -4       | 1.78     | IV                               | Y                  | Y                                             | TKA                | 1                             |
| 20* | III           | M          | -3       | 2.64     | III                              | N                  | Y                                             | TKA                | 1                             |
| 21  | III           | M          | -4       | 1.96     | IV                               | Y                  | N                                             | TKA                | 4                             |
| 22  | IV            | M          | -5       | 1.01     | IV                               | Y                  | N                                             | TKA                | 4                             |
| 23  | IV            | M          | -5       | 0.66     | IV                               | Y                  | Y                                             | TKA                | 1                             |
| 24* | III           | M          | 2        | 3.88     | II                               | N                  | Y                                             | TKA                | 1                             |
| 25* | III           | M          | 1        | 3.20     | II                               | N                  | Y                                             | TKA                | 1                             |
| 26  | IV            | M          | -5       | 0.98     | IV                               | Y                  | Y                                             | TKA                | 1                             |
| 27* | III           | M          | 0        | 2.34     | III                              | N                  | Y                                             | TKA                | 1                             |
| 28  | III           | M          | -4       | 1.44     | IV                               | Y                  | N                                             | TKA                | 2                             |
| 29  | IV            | M          | -10      | 0.00     | IV                               | Y                  | N                                             | TKA                | 1                             |
| 30  | IV            | M          | -3       | 1.56     | IV                               | Y                  | N                                             | TKA                | 3                             |

Comp. = compartment, FTA = femorotibial angle, JSW = joint space width, Post-op. = post-operative, Pre-op. = pre-operative, TKA = total knee arthroplasty, UKA = unicompartmental knee arthroplasty.

* Denotes cases with earlier arthroscopic grading of II or III and without meniscus protrusion.

Figure 3. An example of the reversal of the degeneration process after receiving ACRFP. (a) AP standing view of a 69-year-old female patient having Stage V OA over medial compartment of her left knee and Stage III OA over medial compartment of her right knee, unicompartmental arthroplasty for her left knee and ACRFP for her right knee was recommended; (b) 39 months later, obvious improvement of the radiographic manifestation could be observed for both of her knees. ACRFP = arthroscopic cartilage regeneration facilitating procedure, OA = osteoarthritis.
in time, ACRFP combined with skillful post-operative self-rehabilitation has demonstrated that reestablishing a favorable biomechanical environment for knees may satisfy most patients with knee OA and delay or avoid the need for invasive joint reconstruction procedures. However, further investigations are needed to confirm this hypothesis.

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References
[1] Marsh JD, Birmingham TB, Giffin JR, et al. Cost-effectiveness analysis of arthroscopic surgery compared with non-operative management for osteoarthritis of the knee. BMJ Open. 2016;6:e009949.
[2] Ruiz D, Koenig L, Dall TM, et al. The direct and indirect costs to society of treatment for end-stage knee osteoarthritis. Bone Jt Surg - Ser A. 2013;95:1473–80.
[3] Lyu SR, Hsu CC. Medial plicae and degeneration of the medial femoral condyle. Arthroscopy. 2006;22:17–26.
[4] Lyu SR, Tzeng JE, Kuo CY, et al. Mechanical strength of mediopatellar plica – the influence of its fiber content. Clin Biomech (Bristol Avon). 2006;21:860–3.
[5] Lyu SR. Relationship of medial plica and medial femoral condyle during flexion. Clin Biomech (Bristol Avon). 2007;22:1013–6.
[6] Lyu SR, Chang JK, Tseng CE. Medial plica in patients with knee osteoarthritis: a histomorphological study. Knee Surg Sports Traumatol Arthros. 2010;18:769–76.
[7] Wang HS, Kuo PY, Yang CC, et al. Matrix metalloprotease-3 expression in the medial plica and pannus-like tissue in knees from patients with medial compartment osteoarthritis. Histopathology. 2011;58:593–600.

[8] Yang CC, Lin CY, Wang HS, et al. Matrix metalloproteases and tissue inhibitors of metalloproteinases in medial plica and pannus-like tissue contribute to knee osteoarthrits progression. PLoS One. 2013;8:e79662.

[9] Liu DS, Zhuang ZW, Lyu SR. Relationship between medial plica and medial femoral condyle – a three-dimensional dynamic finite element model. Clin Biomech (Bristol Avon). 2013;28:1000–5.

[10] Lyu SR, Chang CY, Cherng JY, et al. Role of medial abrasion phenomenon in the pathogenesis of knee osteoarthritis. Med Hypotheses. 2015;85:207–11.

[11] Lyu SR. Arthroscopic medial release for medial compartment osteoarthritis of the knee: the result of a single surgeon series with a minimum follow-up of four years. J Bone Joint Surg Br. 2008;90:1186–92.

[12] Lyu SR, Hsu CC, Lin CW. Arthroscopic cartilage regeneration facilitating procedure for osteoarthritic knee. BMC Musculoskelet Disord. 2012;13:226.

[13] Lyu S-R. Knee health promotion option for knee osteoarthritis: a preliminary report of a concept of multidisciplinary management. Heal Ageing Res. 2015;4:34.

[14] Mediouni M, Schlatterer D R, Madry H, et al. A review of translational medicine. The future paradigm: how can we connect the orthopaedic dots better? Curr Med Res Opin. 2018;27:1–26.

[15] Slattery C, Kweon CY. Classifications in brief: outerbridge classification of chondral lesions. Clin Orthop Relat Res. 2018;476:2101–4.

[16] Joseph GB, Baum T, Carballido-Gamio J, et al. Texture analysis of cartilage T2 maps: individuals with risk factors for OA have higher and more heterogeneous knee cartilage MR T2 compared to normal controls – data from the osteoarthritis initiative. Arthritis Res Ther. 2011;13:R153.

[17] Peterfy CG, Guermazi A, Zaim S, et al. Whole-organ magnetic resonance imaging score (WORMS) of the knee in osteoarthritis. Osteoarthritis Cartilage. 2004;12:177–90.

[18] Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. Br J Anaesth. 2013;111:52–8.

[19] Bernhard JC, Vunjak-Novakovic G. Should we use cells, biomaterials, or tissue engineering for cartilage regeneration? Stem Cell Res Ther. 2016;7:56.

[20] Koshino T, Wada S, Ara Y, et al. Regeneration of degenerated articular cartilage after high tibial valgus osteotomy for medial compartmental osteoarthritis of the knee. Knee. 2003;10:229–36.

[21] Kanamuya T, Naito M, Hara M, et al. The influences of biomechanical factors on cartilage regeneration after high tibial osteotomy for knees with medial compartment osteoarthritis: clinical and arthoscopic observations. Arthroscopy. 2002;18:725–9.

[22] Davison T, Kunig S, Chen A, et al. Static and dynamic compression modulate matrix metabolism in tissue engineered cartilage. J Orthop Res. 2002;20:842–8.

[23] Sharma G, Saxena RK, Mishra P. Differential effects of cyclic and static pressure on biochemical and morphological properties of chondrocytes from articular cartilage. Clin Biomech (Bristol Avon). 2007;22:248–55.

[24] Waller C, Hayes D, Block JE, et al. Unload it: the key to the treatment of knee osteoarthritis. Knee Surg Sports Traumatol Arthosc. 2011;19:1823–9.

[25] Chen Y, Sun Y, Pan X, et al. Joint distraction attenuates osteoarthritis by reducing secondary inflammation, cartilage degeneration and subchondral bone aberrant change. Osteoarthritis Cartilage. 2015;23:1728–35.

[26] Wu TC, Yen CH, Lyu SR, et al. Modification in foot pressure and gait pattern after arthroscopic cartilage regeneration facilitating procedures (ACRFP) in patients with osteoarthritis of knee. J Mech Med Biol. 2019;19:1940026.

[27] Moseley JB, O’Malley K, Petersen NJ, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med. 2002;347:81–8.

[28] Laupattarakasem W, Laopaiboon M, Laupattarakasem P, et al. Arthroscopic debridement for knee osteoarthritis. Cochrane Database Syst Rev. 2008;1:CD005118.

[29] Mithoefer K, Mcadams T, Williams RJ, et al. Clinical efficacy of the microfracture technique for articular cartilage repair in the knee: an evidence-based systematic analysis. Am J Sports Med. 2009;37:2053–63.

[30] Thorlund JB, Juhl CB, Roos EM, et al. Arthroscopic surgery for degenerative knee: systematic review and meta-analysis of benefits and harms. Br J Sports Med. 2015;49:1229–35.