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| Original Article |

Comparison Between Total Knee Arthroplasty and MCIC (autologous bone marrow mesenchymal-cell-induced-chondrogenesis) for the Treatment of Osteoarthritis of the Knee

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Abstract : Total knee arthroplasty (TKA) is the gold standard of treatment for advanced osteoarthritis of the knee. The technical methods of cartilage regeneration procedures are now well-developed. Indications for this procedure are being expanded to the treatment of osteoarthritis. We compared data from 42 patients who underwent TKA and from 52 patients who underwent MCIC (autologous bone marrow mesenchymal-cell-induced-chondrogenesis). All patients were over 50 years of age and showed grade IV of the Kellgren-Lawrence classification. The TKA patients were older and predominantly female, compared to the MCIC patients. There was no difference between the two groups regarding the patient satisfaction. Clinical evaluation of the two groups showed significant mean improvement in the tKSS-A (pain) and tKSS-B (function) scores throughout the postoperative follow-up period. The monetary cost of TKA was relatively higher than that of MCIC. Therefore, considering the patient age and quality of life, MCIC is a potential treatment option for osteoarthritis as it thus delays the disease progression.

Key words: *osteoarthritis, total knee arthroplasty, cartilage regeneration, MCIC, hospital fee*

1. Introduction

As the human life span is increasing with the improvement of medical standards and the standard of living, there is a concomitant increase in the incidence of degenerative disease.[1] As degenerative knee joint disease greatly impacts the quality of life, there is an increasing focus on the prevention and treatment of arthritis.[2]

According to a study published by the US National Library of Medicine National Institutes of Health, the demand for primary total knee arthroplasty (TKA) is projected to increase by 673% between 2005 and 2030.[3] Based on this report, we can correctly assume that the development of biologic treatment, such as cartilage regeneration, is necessary and important for the treatment of osteoarthritis. In response to this necessity, many treatment methods based on arthroscopic surgery have been developed and attempted in recent decades. [4,5]

However, TKA still remains the gold standard for the treatment of severe osteoarthritis. In general, arthroplasty has a defined life span and revisional arthroplasty surgery is necessary 10 to 15 years after the primary arthroplasty. [6]

As the survival rate of primary TKA in younger patients is a cause of concern, especially due to the higher rates of aseptic failure, in such patients knee revision may be necessary once or twice during their lifetime.[6, 7] Patients over 50 or 60 years of age require at least one revisional surgery, considering the tendency of the increasing human life span.

This increased incidence of revisional surgery can cause an immense personal and socio-economic burden. The arthroscopic cartilage regeneration procedure (CRP) with microfracture using scaffolds or stem cells is one of the representative alternate surgeries to TKA.[8, 9]

Autologous bone-marrow, mesenchymal-cell-induced chondrogenesis (MCIC) is one of the representative CRPs and it

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is a single stage, arthroscopic surgery.[9,10] This technique uses microfracture, BMAC, HA, and fibrin gel to treat articular cartilage defects, and a recent, two-year follow-up study showed significant clinical and radiological improvement.[10]

Given this background, we compared the clinical results and hospital costs of TKA and MCIC using arthroscopic microfracture followed by injection of a mixture of bone marrow concentrate and fibrin.

2. Patients and Methods

2.1 Patients

We included data from 42 patients who underwent TKA and from 52 patients who underwent MCIC between June 2011 and September 2013 at a single medical center. Among the 42 TKA patients, there were three males (7.1%), and 39 females (92.9%), and there were 15 bilateral TKA patients (35.7 %). Among the 52 MCIC patients, there were 16 males (30.8%), and 36 females (69.2%), and there were 18 bilateral MCIC patients (15.4%). The TKA patient age range was from 57 to 80 years (mean age = 70.02 years, SD = 5.87). The MCIC patient age range was from 50 to 73 years (mean age = 57.96 years, SD = 4.83).

The average follow-up period was 14 months (range: 6 ~ 31 months) for TKA patients and 19 months (range: 7 ~ 32 months) for MCIC patients (Table 1).

Table 1. General Description N=94

Characteristics	TKA (n=42)	MCIC (n=52)	*p*
	n (%) or mean (±SD)		
Age	70.0 (±5.9)	58.0 (±4.8)	
50~59	2 (4.8)	34 (65.4)	.00*
60~69	15 (35.7)	17 (32.7)	
70~80	25 (59.5)	1 (1.9)	
Gender			
Male	3 (7.1)	16 (30.8)	.01†
Female	39 (92.9)	36 (69.2)	
Defect side			
Right	13 (31.0)	25 (48.1)	.06†
Left	14 (33.3)	19 (36.5)	
Both	15 (35.7)	8 (15.4)	
Elapsed months	14.0 (±6.7)	18.7 (±5.6)	
~11month (under 1 yr)	19 (45.2)	5 (9.6)	.00*
~23month (under 2 yrs)	17 (40.5)	35 (67.3)	
24month~ (more than 2 yrs)	6 (14.3)	12 (23.1)	
Patient satisfaction	1.5 (± .7)	1.5 (± .7)	1.00*

*: Independent test, †: chi-square test were performed
TKA: total knee arthroplasty; MCIC (autologous bone marrow mesenchymal-cell-induced chondrogenesis)

There was no additional surgery, including TKA or high tibial osteotomy, required during the follow-up period. This study was approved by the Institutional Review Board of The Catholic University of Korea.

2.2 Evaluation of Patient Suitability for Study Participation (inclusion and exclusion criteria)

All included patients were over 50 years of age and showed grade IV of the Kellgren-Lawrence classification in the radiographs of weight bearing standing AP as well as 45-degree flexion PA. The knee joint was required to be stable and without a severe deformity of >10 degrees of the valgus or varus in the mechanical femorotibial angle of both lower extremities, as seen on standing AP radiographs.

All included patients had shown no clinical improvement in response to at least six months of previous conservative treatments, including medication, intra-articular injection, and physical therapy. All surgeries were performed by a single surgeon.

The exclusion criteria included early osteoarthritis (Kellgren-Lawrence Grading Scale < 3) and inflammatory arthritis with severe deformity, exceeding the above-mentioned range, patellofemoral instability, >10 degree of flexion contracture, drug abuse history, and psychological problems.

2.3 Surgical Technique

2.3.1 Cartilage regeneration

1) Harvesting of bone marrow

After administering anesthesia, the patient's anterior superior iliac spine (ASIS) was marked, cleaned, and draped. A bone-marrow aspiration needle (SPASY™, CYP Biotech, Seoul, Korea) and syringes pre-loaded with 2 mL Anticoagulant Citrate Dextrose solution (Huons ACD Injection, Huons, Seongnam, Korea) were used to aspirate 30 mL of bone marrow from the iliac crest. The aspiration site was injected with a local anesthetic and covered with a sterile plaster. The bone-marrow aspirate was then centrifuged twice (Tricell BMC kit/CCR kit, CYP Biotech & REV-MED, Seoul, Korea) (Fig 1a). The first cycle was for six minutes at 3500 rpm, followed by the second cycle for five minutes at 3300 rpm, in order to obtain BMAC (bone-marrow aspirate concentrate).

2) Preparation of BMAC, HA, and the fibrin gel mixture

For application to the chondral defect, two, 1 mL syringes were connected to a Y-shaped mixing catheter. One syringe contained 0.8 mL of fibrinogen (GreenPlast™, Greencross, Seoul, Korea) and 0.2 mL of hyaluronic acid (Highhyal, Huons, Seoul, Korea). The second syringe contained 0.8 mL of bone-

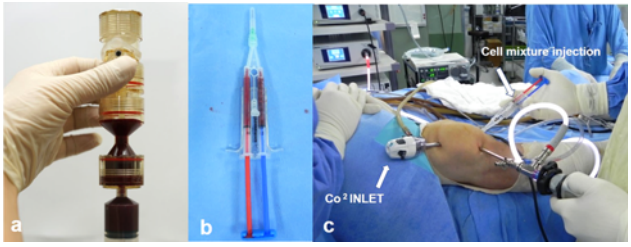

Figure 1. (a) BMAC harvesting and concentration (CCR kit). (b) Double syringe with concentrated BMAC and thrombin/fibrinogen gel. (c) Arthroscopy and CO_2 infusion setup. Graft after application.

marrow concentrate and 0.2 mL of thrombin (Greenplast™, Greencross, Seoul, Korea) (Fig 1b).

3) Arthroscopic procedures for arthritis

The knee was approached *via* the antero-lateral and antero-medial arthroscopic portals, and normal saline was infused under pressure (approximate to systolic blood pressure). A Wolf cannula (Karl Storz GmbH, Tuttlingen, Germany) was inserted superolaterally as an outflow cannula (Fig 1c). The knee joint was systematically assessed, and the arthritic lesions were identified, assisted by pre-operative scans. The arthroscopic arthritis treatment procedures included osteophyte removal, meniscectomy of torn and deformed menisci, if observed, synovectomy, and careful debridement using curettes and shavers for the arthritic chondral surface; burrs were used to remove the sub-chondral sclerotic surface. Microfracture was performed by awl (Arthrex Inc, Naples, FL, USA) to a depth of 3 mm, at intervals of 3 mm (Fig 2a).

4) Application of BMAC, HA, and fibrin-gel mixture

The saline was drained from the knee joint and carbon dioxide (CO_2) was introduced at 20 mm Hg, at a rate of 20 l/per minute using the Wolf cannula (Karl Storz GmbH, Tuttlingen, Germany) and disposable tubing with a filter (Insufflation tubing with a Wolf adaptor, Leonhard Lang UK Ltd., Stroud, UK) through the superolateral portal. Residual saline was aspirated from the knee using both a 20-mL syringe and an angled suction tube under low pressure in order to avoid bleeding. The microfractured lesion(s) was/were dried using cotton buds. A 20-gauge needle (inner diameter 0.9 mm, length 90 mm) (Spinal needle, Becton Dickinson, Madrid, Spain) was inserted into the joint *via* any suitable portal and was connected to the double syringe. Under arthroscopic guidance, the BMAC, HA, and fibrin-gel mixture were gently applied *via* the double syringe and uniformly over the lesion (Fig 2b). For patello-femoral joint lesions, a patellar clamp (AO or Lewin bone clamp) was used to lift and stabilize the patella. Due to the tamponade effect of the CO_2 and the adhesiveness of the gel, the graft adheres to the lesion(s), even against gravity. If necessary, a second layer was injected deep into the firm first layer. The graft could be shaped *in situ* using a McDonalds dissector (Bolton Surgical, UK). The graft became firm after five minutes and under arthroscopic vision. The knee was then moved several times through its range of motion in order to anatomically sculpt the graft and test its stability. If satisfactory, the CO_2 was switched off and all instruments were withdrawn. The portal sites were injected with local anesthetic (0.5% Chirocaine) and closed with sutures. The knee was covered with a compression bandage.

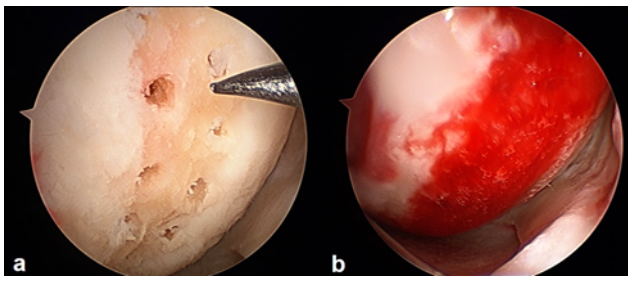

Figure 2. (a) Microfracture procedure. (b) Graft after application.

2.3.2 Total knee-joint replacement arthroplasty

TKA was performed through the midline skin incision and using the medial parapatellar approach. The implants were of the posterior, stabilized type (Lospa, Corentech, Seoul, Korea), and the femoral and tibial components were fixated by cement. The patella was not replaced.

2.4 Rehabilitation

Use of continuous, passive-motion (CPM) machines was begun for rehabilitation from day 1 post-surgery in both groups. Quadriceps muscle-strengthening exercise was continued during the pre- and post-surgery period. For TKA patients, partial weight–bearing, walking exercise with a crutch or walker was begun on the second day post-surgery and was followed by full weight-bearing, according to the patient comfort. For MCIC patients, partial weight-bearing walking exercise with a crutch or walker was begun on the second day post-surgery and was followed by full weight-bearing beginning 6~8 weeks post-operatively. The weight bearing was protective of the surgery site, and excessive weight to the lesion was prevented in order to assist in the cartilage regeneration. CPM was used for 30 minutes on the first day post-surgery and with daily increments of 10 minutes up to a total of four hours per day.

2.4.1 Patient evaluations

- Clinical evaluation.

Details concerning the patients' clinical outcomes were

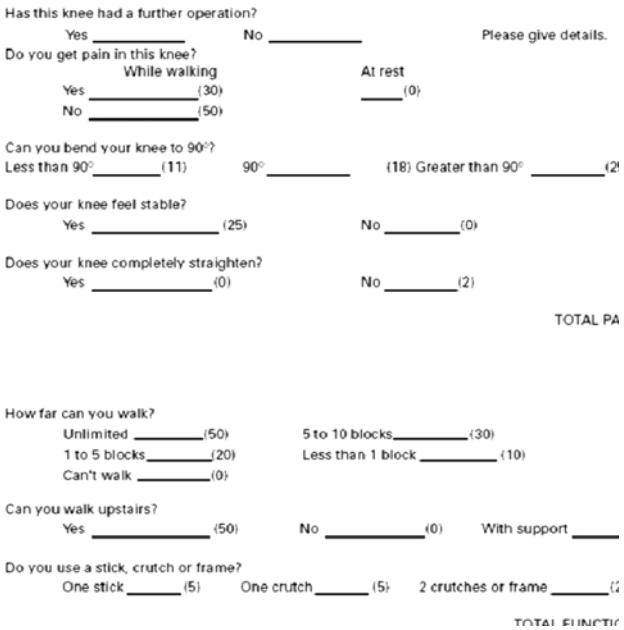

Figure 3. The telephone score format used to estimate the KSS.

collected using the telephone score format initially used to estimate the KSS (Fig 3). [11] The above information was obtained pre-operatively and during the telephone follow-up post-operatively.

Our clinicians rated the patient knee status using the standardized 100-point rating scale of the telephone Knee Society Scoring system (tKSS) regarding pain (A) and function (B) (Fig 3). Adverse event data were collected and included in the analysis, regardless of relatedness to the surgery.

- Hospital fee analysis

The available hospital fee data from 26 TKA(Total Knee Arthroplasty) and 46 MCIC patients have been analyzed.

2.5 Statistical Analysis

Categorical variables were presented as numbers and percentages, and continuous variables were expressed as mean±SD and range. Categorical variables were analyzed using the chi-square test. The nonparametric Wilcoxon signed rank test was used for the comparison of means between the two groups based on the result of test of normality.The Mann-Whitney *U* test was used for the general mean comparison between the two groups. For parametric test, the mean comparison between two groups was done by independent test. To deduce the pattern and relative influence among the variables, categorical variables after Dummy parameterization were analyzed using the Enter method Multiple regression analysis, Two-way ANOVA & Scheffe Post Hoc test.

The T-test was conducted to compare the hospital fees for single TKA and MCIC. The T-test could not be conducted for bilateral procedures because of a lack of cases.

SPSS software version 14.0 (SPSS Inc, USA) was used for statistical analyses.

3. Results

TKA patients were older than MCIC patients and females were predominant. There was no difference between the two groups in the patients' satisfaction (Table 1). Clinician evaluations in two groups showed significant mean improvement in the tKSS-A (pain) and tKSS-B(function) scores for the all the post-operative data throughout the follow-up period (Table 2).

There was no difference in the degree of improvement between the two groups (Table 3). In the analysis of the relative influence of patient characteristics and treatments on the improvement of pain, function, and satisfaction, only age variable showed a contrary relationship (p= .01). The younger age showed better pain improvement and other variables (sex, side of lesion, treatment method) showed no effect on the pain, function, and satisfaction (Table 4).

The age variable was divided into 3 groups according to the

Table 3. The Pre-post Difference in Pain and Function in Each Treatment Group N=94

Type of treatment	Pre-post pain difference	*p* *	Pre-post function difference	*p* *
	Mean (±SD)		Mean (±SD)	
TKA (n=42)	63.3 (20.6)	.25	44.4 (29.6)	.17
MCIC (n=52)	66.6 (21.1)		53.4 (29.4)	

* Mann-Whitney test was performed

Table 2. Overall Pain and Function Scores N=94

Group	Pre-pain	Post-pain	*p**	Pre-function	Post-function	*P**
	Mean(±SD)			Mean(±SD)		
TKA (n=42)	25.8(13.5)	89.1(11.4)	.00	38.8(20.3)	83.2(17.3)	.00
MCIC (n=52)	24.8(15.4)	91.4(14.0)	.00	33.4(26.1)	86.7(18.8)	.00
Total	25.2(14.5)	90.4(12.9)	.00	35.8(23.7)	85.2(18.1)	.00

* Wilcoxon signed rank test was performed

Table 4. Effect of Variables on Pre-post Difference and Patient Satisfaction N=94

Variables	Pre-post Pain difference			Pre-post Function difference			Patient Satisfaction		
	β	SE	p^*	β	SE	p^*	β	SE	p^*
Age	-.40	.40	.01	-.04	.59	.80	.02	.01	.90
Gender									
Male	-.14	5.52	.20	-.13	8.16	.26	.07	.19	.55
Female (reference)									
Defect side									
Right	.16	5.56	.23	.07	8.21	.61	-.05	.19	.72
Left	.17	5.63	.19	-.04	8.32	.79	-.02	.20	.89
Both (reference)									
Treatment									
MCIC	-.21	6.68	.19	.15	9.86	.38	-.00	.23	.98
TKR (reference)									

* Enter method Multiple regression analysis was performed

Table 5. Two-way ANOVA Results for Pain Differences N=94

Source	SS	Df	MS	F	p^*
Treatment	631.14	1	631.14	1.62	.21
Age grade	1918.93	2	959.47	2.47	.09
Treatment X Age grade	105.22	2	52.61	.14	.87
Error	34236.12	88	388.88		
Total	438807.00	94			

* Two-way ANOVA, Scheffe Post-Hoc test was performed

Table 7. Two-way ANOVA Results for Post-op Function N=94

Source	SS	df	MS	F	p^*
Treatment	146.63	1	146.63	.46	.37
Elapsed Year	639.19	2	319.60	.10	.50
Treatment X Elapsed Year	1600.10	2	800.05	2.50	.09
Error	28215.12	88	320.63		
Total	712225.00	94			

* Two-way ANOVA was performed

previous regression analysis. The improvement of pain showed a difference in age groups (p=.09). The post-hoc comparison was done by the Scheffe test. Less than 60 years old patients showed a better improvement in pain relief than over 70 years old patients with no difference between two treatment methods (Table 5).

The pain and functional improvement of each treatment method according to the follow up period were significantly different (p=.03). MCIC showed improved pain and function according to the follow up period but not TKA (Table 6, 7).

The T-test analysis for single procedures showed that the medical charges for most TKA items were relatively higher than those for MCIC (Table 8). There were significant differences in average hospital fees per person, the corporate contribution, the personal contribution, the benefit insurance payment, and the special doctor's fee. The non-benefit insurance payment alone was not different between TKA and MCIC. The average hospital fee per patient for single TKA was 43.3% (2,039.4$) more expensive, than that for MCIC.

Table 6. Two-way ANOVA Results for Post-op Pain N=94

Source	SS	df	MS	F	p^*
Treatment	77.97	1	77.97	.49	.49
Elapsed Year	283.16	2	141.58	.89	.42
Treatment X Elapsed Year	1131.85	2	565.93	3.55	.03
Error	14042.69	88	159.58		
Total	783022.00	94			

* Two-way ANOVA was performed

The medical insurance corporate contribution was the amount paid to the hospital from the Korean National Health Insurance Corporation according to the Korean National Medical Insurance System, and the patient's personal contribution was the medical charge that a patient pays to the hospital. Total hospital fees are the sum of the corporate contribution and personal contribution. As a result, the corporate contribution for single knee TKA was 46.6% ($1,446.00) more expensive than that for MCIC. The personal contribution for the TKA was 36.8% (594.4$) more expensive than that for MCIC.

The benefit insurance payment is the total hospital fees payable by National Health Insurance, and the non-benefit insurance payment is the hospital fees not covered by the National Health Insurance. A special doctor fee was the hospital fee paid when a

Table 8. T-test Results According to Each Hospital's Fees (USD)

	One knee procedure		t-test
	TKA (N=26)	MCIC (N=46)	
Average hospital fee per patient	6,754.0$ (± 1,073.8$)	4,714.6$ (± 3,260.6$)	3.89***
Corporate contribution	4,546.4$ (± 692.9$)	3,100.4$ (± 2,503.6$)	2.88**
Personal contribution	2,207.6$ (± 464.4$)	1,613.2$ (± 1,053.9$)	3.30**
Benefit insurance payment	5,683.0$ (± 866.1$)	3,875.4$ (± 3,129.5$)	2.88**
Non-benefit insurance payment	412.5$ (± 363.2$)	285.0$ (± 786.2$)	0.78
Special doctor fee	658.4$ (± 151.5$)	553.0$ (± 161.3$)	2.72**

*P<.05 **P<.01 ***P<.001

The exchange rate for the hospital fees of Korean won for US dollars was 1,095.04 won per dollar according to the annual average sales basic rate in 2013.

Table 9. T-test Results for Itemization of the Medical Charges (USD)

	One knee procedure		t-test
	TKA (N=26)	MCIC (N=46)	
Doctor's fee	31.6$ (± 18.4$)	24.2$ (± 20.8$)	1.46
Patient's room charge and management costs	1,297.1$ (± 599.4$)	1,924.4$ (± 2,374.3$)	1.81
Drug and injection charges	717.0$ (± 189.2$)	568.7$ (± 192.9$)	2.82**
Treatment and operating charges	3,249.3$ (± 214.9$)	994.1$ (± 483.7$)	22.11***
The medical checkup charge	460.6$ (± 245.2$)	349.7$ (± 349.7$)	1.35
The other charges	1,086.6$ (± 128.1$)	802.4$ (± 323.6$)	4.53***

*P<.05 **P<.01 ***P<.001

The exchange rate for the hospital fees of Korean won for US dollars was 1,095.04 won per dollar according to the annual average sales basic rate in 2013.

patient selected a specialist. Total medical expenses were the sum of the benefit insurance payment, the non-benefit insurance payment, and the special doctor fee.

The results showed that the benefit insurance payment for a single TKA surgical procedure was 46.6% ($1,807.60) more expensive than that for MCIC.

The special doctor fee for single TKA was 19.1% ($105.40) more expensive than that for MCIC.

A patient's room charge and management costs included the nursing management cost, the patient's room charge, and meal charges. The drug and injection charges include the drug, injection, and administration fees (Table 9).

The treatment and operating charges included anesthesia, radiographic diagnosis and therapy, neuropsychiatric therapy, rehabilitation and physical therapy, medical materials, and operating expenses. The medical checkup charges were the costs for ultrasonic examinations, magnetic resonance imaging examinations, and other examination charges. The other charges included the amount for patient registration, certificate cost, and the transfer fee.

Drug and injection charges, treatment and operating charges, and the other charges were significantly higher for single TKA than those for MCIC. No differences were observed between TKA and MCIC for doctor's fees, patient room charge, management costs, and the medical checkup charge.

The drug and injection charges for single TKA were 26.1% ($148.30) more expensive than those for MCIC, and the treatment and operating charges for TKA were 226.9% ($2,255.20) more expensive than those for MCIC. TKA was 35.4% ($284.20) more expensive than that for MCIC, for the other charges.

3.1 Adverse events

There was no adverse event.

4. Discussion

As life span increases, the current understanding that the quality of life should supersede longevity has become clearer. Musculoskeletal support should be guaranteed, for healthy living. Knee joint osteoarthritis is one of the most common diseases among musculoskeletal problems; and early treatment of the osteoarthritis is the key to delay disease progression.[12]

Articular cartilage has a limited regenerative potential and it is commonly accepted that injured joint with articular cartilage defect typically progress to osteoarthritis.[13, 14]

For the treatment of advanced osteoarthritis with severe deformity and pain, TKA is the treatment of choice with very high patient satisfaction.[15, 16] TKA can have satisfactory results by the improvement of surgical technique and development of instruments.[17, 18] The number of TKA operation is increasing due to the extended life span and its satisfactory results.[3, 18] However, the concerns and priorities of patients and surgeons differ and it is difficult to evaluate patient's subjective satisfac-

tion.[19] Since many patients suffer from continuous pain after TKA, and the revisional surgery findings reveal abnormal tissue formation, osteolysis, various inflammations, we accordingly tried to find an alternative treatment for osteoarthritis.[20]

Infection, periprosthetic fracture, implant loosening, malalignment, ligament rupture, instability, joint stiffness, and pain are among the post-operative complications of TKA.[21] These complications require specific treatments ranging from medication to re-operation. Some patients are reluctant to receive TKA due to these complications.

Cartilage regeneration operations are based on the arthroscopic marrow stimulation procedure such as microfracture or multiple drilling. Microfracture is a technique which covers injured articular cartilage through the proliferation and differentiation of the mesenchymal cells from the bone marrow.[22] Microfracture treatment is simple, minimally invasive through arthroscopy, and a cost effective first-line treatment option for focal cartilage defects.[23]

The theoretical basis of this procedure is that the hematoma from the penetrated bone marrow contains marrow stromal cells including mesenchymal stem cells, and stem cells that differentiate into chondrocytes and synthesize cartilage.

However this operation is successful in the case of focal cartilage defect or small sized lesion.

For larger lesions, incomplete coverage of the lesion and mechanically weak fibrocartilaginous tissue can be generated. The symptom of patients can recur during rehabilitation, due to damage of the newly formed cartilage.[24]

Therefore, some clinical trials have attempted a transplant of scaffold and a concentrate of bone marrow or fat tissue - derived cells to the damaged articular cartilage, with an increased cartilage regeneration efficacy.[8, 25]

In this study, a mixture of concentrated bone marrow cells, hyaluronic acid and fibrin were used, after arthroscopic microfracture, for cartilage regeneration. The newly introduced operation technique involved the injection of the mixture into the cartilage lesion, under continuous CO_2 inflation without another skin incision, with the aim of promoting a fast recovery.

To maximize the microfracture effect, we additionally injected concentrated bone marrow cells to expand the population of cells that could participate in articular cartilage regeneration, as compared to microfracture alone.

Hyaluronic acid is an important component of articular cartilage. It improves repair potential leading to a more hyaline-like repair tissue, with better defect fill and adjacent area integration.[26] Fibrin is very safe and is routinely used for hemostasis in the surgical field. Fibrin has also been introduced as a main scaffold for cell therapy.[25, 27]

Continuous CO_2 inflation improves the technical aspects of microfracture tremendously.[8] With this technique, a large skin incision is no longer necessary to implant the biologic scaffold to the lesion, since the cartilage of patella and posterior femoral condyle can be accessed without difficulty. Intraarticular positive pressure of CO_2 gas facilitated the attachment of the injected mixture to the articular surface, and fibrin caused the moulding of the mixture in shape and position *via* the action of fibrinogen and thrombin, thus a new articular surface could be formed.[8]

TKA is undoubtedly the most effective treatment for advanced cases of osteoarthritis. However, whether osteoarthritis without severe deformity can be treated by CRP *vs.* TKA is still controversial.[28]

One of the limitations of this study is that both patient groups' age and sex distributions differ. Naturally, younger patients tend to be in the MCIC group undergoing the cartilage regeneration procedure and older patients more often undergo total knee arthroplasty. To compare both treatments more exactly, it is appropriate to perform the study focusing only on a certain age group.

However, for the initial comparative study, this discrepancy is also an important observation point regarding the patient distribution according to the treatment options.

Most clinicians currently prefer the passive treatment option including medication or activity restriction until the injured knee reaches an advanced osteoarthritis to perform TKA, the so called gold standard of osteoarthritis treatment.

The previously defined optimal age for TKA, is over 60 years.[29] There is a high population of people aged over 60 or 70 years, who live healthy and active lives, and expect a high quality of medical service. The advanced medical service such as cartilage regeneration is being performed very actively. [8, 25]

Under these circumstances, the cost effectiveness for TKA and MCIC becomes important. According to Korean National Medical Insurance System, the medical charges for most TKA items were relatively higher than those for MCIC (Table 9). The T-test analysis showed that both the corporate contribution and the personal contribution in the average hospital fees per person for TKA were more expensive than those for MCIC (Table 8). If clinical outcomes and patient satisfactions are not significantly different between TKA and MCIC for the treatment of ostreoarthritis of knee, MCIC rather than TKA, could be a better choice economically for the patients and the Korean National Medical Insurance Corporations.

The most important point of this study is that a cartilage

regeneration procedure such as MCIC can be a treatment option for osteoarthritis without severe deformity and with effectiveness and low cost. This study might be an important clue for making the paradigm shift from total joint replacement surgery to cartilage regeneration treatment for the treatment of osteoarthritis because biological treatment for osteoarthritis is a dream for all clinicians and researchers.

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