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A Retrospective Chart Review of 122 Inpatients with Knee Osteoarthritis Treated with Korean Medicine: An Analysis of the Effects of Treatment

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ABSTRACT

Background: Korean medicine treatment was assessed in patients with knee osteoarthritis (OA) according to subgroups of: sex, age, cause of knee OA, body mass index, hospitalization period, history, OA compartment, phenotype, and comorbidity.
Methods: A retrospective review was performed of 122 inpatients who were admitted to the Hospital of Korean Medicine for Korean medicine treatment of knee pain, and were diagnosed with knee OA based on magnetic resonance imaging findings. Analysis of patient subgroups (sex, age, cause of knee OA, body mass index, hospitalization period, history, OA compartment, phenotype, and comorbidity) was carried out and treatments including acupuncture, cupping, pharmacopuncture, herbal medicine, chuna therapy, medicinal steaming therapy, manual therapy, and extracorporeal shock wave therapy were listed. The numeric rating scale (NRS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and 5-level EuroQol- 5 Dimension (EQ-5D-5L) scores were measured before and after treatment to assess the effects of treatment on pain and quality of life.
Results: Seventeen males and 105 females were included in this study. Most patients were in their 60s. In the total study population, NRS, WOMAC, and EQ-5D-5L scores were improved statistically significant when comparing before and after treatment. The NRS and WOMAC scores improved statistically significant in the medial, patellofemoral, medial + patellofemoral, medial + lateral + patellofemoral compartment.
Conclusion: Korean medicine treatment significantly reduced pain, stiffness, and physical dysfunction, and improved the quality of life of patients with knee OA, suggesting that it may be an effective alternative to the current conservative treatments.

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Introduction

The number of patients treated for knee osteoarthritis (OA) per year has increased from 2,200,331 in 2010 to 2,968,567 in 2019. Consequently, the cost of treatment for knee OA ranked 2nd in the total medical care benefit expenses for inpatients, and 5th in the total medical care benefit expenses for outpatients in 2019 [1].

The unclear etiopathogenesis of knee OA limits classification of subgroups of the disease [2]. However, there are distinct subtypes of knee OA, with clear differences in structural degradation and symptoms. Additionally, the different risk factors of the subtypes suggest that each risk factor leads to a different type of knee OA [3]. Recent studies have shown that knee OA is a secondary disease, and subsequently, studies have limited the classification

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of the disease to phenotype. This is still the most widely used subgrouping type [4]. A primary phenotype refers to those patients without a specific cause, and a secondary phenotype is knee OA caused by trauma and developmental, metabolic, endocrine, and other disorders including anterior cruciate ligament (ACL) tears, meniscal tears, and osteochondral lesions [5,6].

OA occurs in 3 compartments (medial, lateral, and patellofemoral) and these may arise either individually or simultaneously. Medial and lateral compartments show different characteristics [3], and differences in pain, stiffness, and physical function were observed in subgroups of patellofemoral alone and multi-compartment OA [7]. Additionally, a retrospective study assigned patients with knee OA into medial, lateral, and patellofemoral compartments and assessed whether partial knee replacement was appropriate in each compartment [8].

The coexisting disorders of knee OA include cardiovascular disease, obesity, and diabetes mellitus. In particular, musculoskeletal comorbidities affect the severity of the symptoms of knee OA [9]. For example, joint effusion is a key clinical sign associated with the development of pain and stiffness [10], and meniscal injury or meniscal ectomy is related to the development of knee OA [11]. Moreover, pain in patients with knee OA is also affected by subchondral bone lesions [12], and bone marrow lesions [13]. In addition, disease progression is also related to bone marrow lesions [13].

Knee OA is characterized by gradual degenerative changes in the joints and commonly affects weight-bearing joints [14]. Increased physical load on the joints stimulates degenerative changes in the joint; thus, a high body mass index (BMI) is a high risk factor for knee OA [15]. The correlation between knee OA and obesity suggest that obesity affects the onset, symptoms, and prognosis of knee OA. Therefore, management of obesity is important for improving symptoms [16].

Knee OA management aims to improve the quality of life (QoL) of patients by reducing pain and increasing mobility [17]. The Osteoarthritis Research Society International guidelines published in 2019 for knee OA core treatments included education about arthritis and structured physical exercise programs with or without dietary weight management [18]. Topical nonsteroidal anti-inflammatory drugs (NSAIDs), cyclo-oxygenase (COX)-2 inhibitors, intra-articular (IA) corticosteroids, and IA hyaluronic acid are also currently recommended for nonsurgical management of knee OA [18]. However, there are some limitations associated with the use of these drugs. NSAIDs may cause gastrointestinal conditions/diseases, such as intestinal bleeding, indigestion, nausea, vomiting, and hypersensitivity (rash) [19]. In comparison, COX-2 inhibitors cause fewer gastrointestinal disorders than general NSAIDs, however, they increase the risk of developing cardiovascular disease [20]. In addition, IA administration of steroids may lead to cartilage destruction, and infections due to repeated injections [21].

In Korea, traditional Korean medicine and Western medicine coexist, and patients can choose to receive either type of medicine or both simultaneously. In Korean medicine, acupuncture, herbal medicine, and pharmacopuncture are used in combination to treat knee OA and have been shown to give synergistic effects [22,23]. These Korean medicine treatments are provided as combination therapy, and a previous study of in patients with knee OA have been shown to be effective [24].

This study aimed to analyze the demographic characteristics, and symptom improvements of 122 patients admitted as inpatients in a Korean medicine hospital and treated for knee OA. To evaluate symptoms the numeric rating scale (NRS), and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were used to determine the levels of pain, and quality of life was measured using the 5-level EuroQol- 5 Dimension (EQ-5D-5L) scores.

Materials and Methods

Patients

Patients who were hospitalized for 4 days or more at the Hospital of Korean Medicine with knee pain between January 2015 and June 2020 were included in this retrospective review study. Magnetic resonance imaging (MRI) was used because it is a more suitable modality compared with an X-ray scan for diagnosing soft tissue damage and other comorbidities associated with OA. Of the 381 patients in the electronic medical records who were diagnosed with knee OA based on MRI findings, 91 patients' chief complaint was not concerning the knee joint, 2 patients had an NRS score less than 4, 146 were hospitalized for less than 4 days, and 20 patients did not complete the questionnaire upon discharge, thus 259 patients were excluded. A total of 122 patients were included in this study (Fig. 1).

Inclusion criteria

Patients in the electronic medical records diagnosed with knee OA based on MRI findings, whose chief complaint was knee pain, whose knee pain NRS score was ≥ 4, and were hospitalized for ≥ 4 days were included in this study.

Exclusion criteria

Patients who had knee pain following a car accident, those patients who had been diagnosed with other serious conditions/diseases around the knee (malignant tumor, fracture, and infection), those who did not complete the questionnaire upon discharge, and those unsuitable for this research, as per the investigator's discretion, were excluded from the study.

Ethics statement

This retrospective study was approved by the institutional review

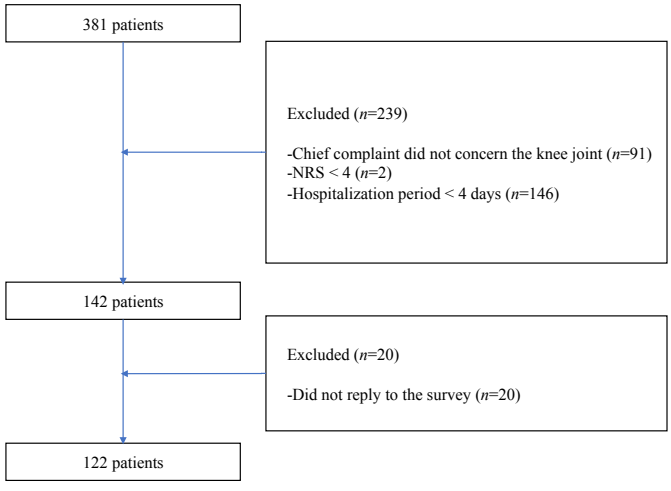

Fig. 1. Flow diagram of patients included in the study.
NRS, numeric rating scale.

board of the Jaseng Hospital and research ethics were adhered to. To protect the patients' personal information, their medical records were accessed after approval from the Institutional Review Board of the Jaseng Hospital of Korean Medicine (no.: 2020-09-014).

Baseline characteristics

Demographic data of the participants included sex and age. The cause of knee OA was divided into 4 categories: (1) unknown; (2) overwork or over-exercise; (3) fall or trauma; and (4) surgery. Based on the Asia-Pacific BMI standards of the World Health Organization, the patients' BMI was divided into underweight/normal/pre-obese/obese Class 1/obese Class 2 [25]. Medical history included hypertension, diabetes mellitus, depression, and cardiovascular, respiratory, gastrointestinal, and musculoskeletal diseases. The OA compartment was classified into medial, lateral, and patellofemoral. The OA phenotype was divided into primary and secondary. Comorbidities included chondral lesions, fluid, meniscus tears, cysts, bone marrow edema, and ACL tears. The distribution of hospitalization length was divided into 7 days.

Treatments

Inpatient treatment included acupuncture, cupping, pharmacopuncture, herbal medicine, chuna therapy, medicinal steaming therapy, manual therapy, and extracorporeal shock wave therapy.

Acupuncture

Stainless steel disposable sterile needles (0.25 × 40 mm) were used for acupuncture treatment (Dong-bang Medical Equipment Manufacturer, Boryung, Korea). Electroacupuncture was performed at 1.0-2.5 cm depth at ST34, SP10, SP9, ST36, ST35, and EX-LE4 acupoints and ashi-points twice a day for 15 minutes each (2-8 Hz).

Cupping

The cups used for cupping were disposable and 37 mm in diameter (Dong-bang Medical Equipment Manufacturer, Boryung, Korea). Wet and dry cupping was performed at BL40 and ashi-points twice daily for 4 minutes each.

Pharmacopuncture

Disposable, single-use, 26-gauge, 13 mm needles with a 1 cc syringe (Sungshim Medical, Bucheon, Korea), filled with 6 cc of refrigerated Shinbaro pharmacopuncture solution (Jaseng herbal medicine dispensary, an extramural facility meeting Korean Good Manufacturing Practice standards) was injected into the acupuncture point (ST35 and EX-LE4) to a needle depth of 0.5-1.0 cm.

Herbal medicine

The patients were prescribed Chungpajun-shinBang No. 2 decoctions (120 mL/package) and Chungshinbaro-Hwan (tablet) 3 times a day (Table 1).

Chuna therapy

The patient underwent chuna therapy once daily. Chuna therapy includes joint mobilization and traction techniques.

Medicinal steaming therapy

Medicinal steaming therapy was administered once daily. Geoseubhwalhyeoljitongtang, which is used to treat musculoskeletal disorders, was placed in a medicine bag, steamed, and placed on the affected knee joint for 15-20 minutes (Table 2).

Manual therapy

The participants underwent manual therapy for up to 40 minutes once a day which was performed by physical therapists under the doctor's instructions.

Extracorporeal shock wave therapy

Extracorporeal shock wave therapy (ESWT) was performed to the participants by a physical therapist under a doctor's prescription for 15 minutes a day.

Table 1. The Herbal Medicine Composition.

Herbal medicines	Herbal components
Chungpajun-shinBang No. 2 (decoction)	Acanthopanacis Cortex 5 g, Eucommiae Cortex 5 g, Saposhnikovia Radix 5 g, Achyranthes bidentata Bl. 5 g, Cibotii Rhizoma 5 g, Atractylodis Rhizoma Alba 2.5 g, Amomi Fructus 2.5 g, Geranii Herba 2.5 g, Zin giberis Rhizoma 1.25 g, Scolopendra morsitans L 0.25 g, Glycyrrhizae Radix 1.6 g
Chungshinbaro-Hwan (tablet)	Poria (Hoelen) 0.15 g, Ginseng Radix 0.07 g, Achyranthes bidentata Bl. 0.04 g, Asini Gelatinum 0.02 g, Rehmanniae Radix 0.62 g, Cervi Cornus Colla 0.06 g, Mel 0.31 g, Cibotii Rhizoma 0.02 g, Eucommiae Cortex 0.02 g, Saposhnikovia Radix 0.01 g, Acanthopanacis Cortex 0.01 g, Scolopendra Corpus 0.01 g, Atractylodis Rhizoma Alba 0.05 g, Atractylodis Rhizoma Alba 0.02 g

Table 2. Medicinal Steaming Therapy Herbal Composition.

Herbal medicines	Herbal components
Geoseubhwalhyeoljitongtang	Cinnamomi Ramulus 3.75 g, Dianthi Herba 3.75 g, Lonicerae Flos 7.5 g, Angelicae Gigantis Radix 3.75 g, Persicae Semen 3.75 g, Akebiae Caulis 7.5 g, Saposhnikovia Radix 3.75 g, Angelicae Dahuricae Radix 3.75 g, Rehmanniae Radix 3.75 g, Sappan Lignum 1.875 g, Linderae Radix 3.75 g, Achyranthis Bidentatae Radix 3.75 g, Clematidis Radix 3.75 g, Coicis Semen 7.5g, Poria 3.75 g, Paeoniae Radix Rubra 3.75 g, Citri Pericarpium 3.75 g, Atractylodis Rhizoma 7.5 g, Cnidii Rhizoma 3.75 g, Gentianae Radix 3.75 g, Polygoni Avicularis Herba 3.75 g, Carthami Flos 1.875 g

Assessment methods

NRS

The extent of knee pain and discomfort was assessed using the NRS which is a subjective pain scale where the patient indicates their pain as a whole number from 0 to 10. where 0 indicates "no pain or discomfort" and 10 indicates "the most severe pain and discomfort imaginable." NRS scores were recorded at admission and discharge from the hospital.

WOMAC

WOMAC is an index for the assessment of pain in patients with OA and is one of the most widely used indexes to assess disorders related to OA pain and joint function. The WOMAC index consists of 3 subdomains with a total of 24 items. Among these, there are 5, 2, and 17 items on pain, stiffness, and physical function, respectively, to evaluate the overall functional capacity of the joints. Each item was evaluated on a 5-point Likert scale (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = extreme) or using 2 types of visual analog scale (a score of 0 to 10 divided into 5 levels). The total points of items on pain, stiffness, and physical function were 0-20, 0-8, and 0-68 points, respectively, and each item was given the same weighted value. The validity of the WOMAC index was validated in 1988 by Bellamy et al [26], whereby scores were recorded at admission and discharge from hospital. In this study, the WOMAC scores were used to evaluate each category (pain, stiffness, and physical function) by comparing before and after treatment between the subgroups.

EQ-5D-5L

The EQ-5D-5L is a method of indirectly calculating the weights of certain health states for QoL after a multidimensional investigation of state of health, and is the most widely used instrument for this purpose [27]. The EQ-5D consists of 5 questions about current health state (mobility, self-care, usual activities, pain, and anxiety/depression), and each question is scored on a 5-point Likert scale (1 = no problems, 2 = slight problems, 3 = moderate problems, 4 = severe problems, 5 = extreme problems). In this study, the Korean version of EQ-5D-5L was used, which has been validated for evaluating knee OA [28]. The EQ-5D-5L scores were recorded at admission and at discharge from hospital.

Data analysis method

Statistical analysis was conducted using SPSS Version 27.0 for Windows (IBM Corporation, USA). Categorical variables, such as baseline characteristics, are presented as frequencies and percentages. Continuous variables are presented as the mean ± standard deviation (SD) of the scores for changes in the NRS, WOMAC index, and EQ-5D-5L index. Comparisons before and after treatment shown in Tables 3-5 were examined for normality before statistical analysis using a paired t test for parametric data and the Wilcoxon signed-rank test for nonparametric data. The differences between groups shown in Tables 3-9 were analyzed by the Student t test when the number of variables was 2, and by the 1-way ANOVA test when the number of variables was more than 3. Statistical significance was reached when p values were < 0.05.

Results

Baseline characteristics

The total number of inpatients was 122, with 17 males and 105 females. The mean age was 63.44 years, with 68 patients in their 60s (55.74%). There were 93 cases (76.23%) with unknown causes and 16 (13.11%) from falls or trauma. The inpatient mean value for BMI was 24.04 (pre-obese). There were 47 cases (38.52%) in the normal range, 31 cases (25.41%) were pre-obese, 37 cases (30.33%) were obese Class 1, and 5 cases (4.10%) were obese Class 2. The distribution of inpatients' medical history consisted of 90 cases (73.77%) of musculoskeletal disease, 35 cases (28.7%) of hypertension, and 26 cases (21.31%) of cardiovascular disease. The distribution of the knee compartment affected by OA, as discovered by MRI findings, included 35 cases (28.69%) in the medial compartment, 24 cases (19.67%) in the patellofemoral compartment, and 43 cases (35.25%) in both the medial and patellofemoral compartments. In the distribution of phenotypes discovered by MRI, there were 118 cases (96.72%) classified as a primary phenotype and 4 cases (3.27%) which were classified as a secondary phenotype. Regarding the distribution of comorbidities with OA, 82 patients had meniscal tears (67.21%), 82 patients had cysts (67.21%), and 81 had a bone marrow edema (66.39%). The mean hospitalization period for all inpatients was 28.16 days (Table 10).

Treatments

The means and SDs of treatment times are shown in Table 11. Korean medicine and physiotherapy treatments are shown as the number of times an inpatient received treatment (Table 12). Spearman's correlation coefficient analysis for the number of treatments and changes in NRS scores were as follows: acupuncture (0.319; $p < 0.001$), herbal medicine (0.298; $p < 0.001$), pharmacopuncture (0.27; $p < 0.01$), chuna therapy (0.275; $p < 0.01$), medicinal steaming therapy (0.308; $p < 0.01$), cupping (0.231; $p < 0.05$), and manual therapy (0.192; $p < 0.05$). The correlation coefficient of ESWT was not statistically significant (Table 13).

Assessments

In a comparison before and after treatment, the NRS score significantly decreased from 5.39 ± 0.85 to 3.60 ± 1.02 ($p < 0.001$), the WOMAC (pain, stiffness, physical function, total) scores significantly decreased from 10.22 ± 3.56 to 7.42 ± 3.14 ($p < 0.001$), 4.09 ± 1.68 to 3.02 ± 1.53 ($p < 0.001$), 37.02 ± 11.43 to 26.16 ± 10.83 ($p < 0.001$), 51.34 ± 15.66 to 36.60 ± 14.68 ($p < 0.001$), respectively, and the EQ-5D-5L score significantly improved from 0.57 ± 0.17 to 0.62 ± 0.02 ($p < 0.05$; Table 14).

The NRS scores before and after treatment were grouped by hospitalization period, sex, age, BMI, history, and comorbidities (Table 3). All NRS scores decreased significantly in each group ($p < 0.001$). When NRS scores were grouped by knee compartment, the medial, the patellofemoral, the medial + patellofemoral, and the medial + lateral + patellofemoral compartment NRS scores decreased significantly. A comparison of the scores from patients with differing hospitalization periods indicated that the decrease in NRS scores was significant in at least 1 group ($p < 0.01$). A comparison of NRS scores between the groups with or without musculoskeletal disease showed a significant difference ($p < 0.01$).

Analyses of the WOMAC scores before and after treatment were grouped by hospitalization period, sex, age, BMI, history, and comorbidities; the scores decreased significantly in each group after treatment ($p < 0.05$). When the WOMAC scores were grouped by knee compartment, the medial, the patellofemoral, the medial + patellofemoral, and the medial + lateral + patellofemoral compartment WOMAC scores decreased significantly ($p < 0.001$) (Table 4).

Analysis of EQ-5D-5L scores before and after treatment is shown

Table 3. Comparison of Knee NRS Scores Before and After Treatment.

		N	Admission		Discharge		Before & after	Between groups
			Mean	SD	Mean	SD	*p*	F(*p*)
Hospitalization period (d)	4-14	29	5.28	0.702	4.00	1.000	< 0.001†	5.093 (0.002)§
	15-28	33	5.27	0.977	3.67	1.109	< 0.001*	
	29-42	37	5.65	0.889	3.41	0.956	< 0.001*	
	43-	23	5.26	0.689	3.30	0.876	< 0.001†	
Sex	Male	17	5.24	0.664	3.59	0.870	< 0.001†	-0.559 (0.577)
	Female	105	5.41	0.874	3.60	1.043	< 0.001*	
Age (y)	40-59	31	5.42	0.923	3.52	0.962	< 0.001*	0.413 (0.663)
	60-69	68	5.31	0.797	3.60	1.010	< 0.001*	
	70-	23	5.57	0.896	3.70	1.146	< 0.001†	
BMI	Normal & underweight	48	5.38	0.866	3.44	1.029	< 0.001*	1.102 (0.336)
	Pre-obese	31	5.39	0.803	3.55	0.961	< 0.001*	
	Obese Class 1 & 2	42	5.40	0.885	3.81	1.042	< 0.001*	
OA compartment	Medial	35	5.26	0.780	3.54	0.886	< 0.001*	
	Lateral	3	6.33	1.528	5.00	1.000	N/A	
	Patellofemoral	24	5.29	0.999	3.17	1.007	< 0.001†	
	Medial + lateral	2	4.50	0.707	3.50	0.707	N/A	
	Medial + patellofemoral	43	5.42	0.763	3.81	1.052	< 0.001*	
	Lateral + patellofemoral	1	6.00	N/A	1.00	N/A	N/A	
	Medial + lateral + patellofemoral	14	5.64	0.745	3.71	0.726	0.001‡	
History	Hypertension	35	5.23	0.731	3.74	0.817	< 0.001*	1.926 (0.056)
	No hypertension	87	5.45	0.886	3.54	1.087	< 0.001*	
	CVD	26	5.27	0.827	3.65	0.936	< 0.001*	0.889 (0.376)
	No CVD	96	5.42	0.854	3.58	1.043	< 0.001*	
	MSD	90	5.37	0.854	3.80	0.914	< 0.001*	3.076 (0.004)‖
	No MSD	32	5.44	0.840	3.03	1.092	< 0.001*	
Comorbidities with OA	Joint effusion	51	5.59	0.853	3.75	1.055	< 0.001*	-0.474 (0.636)
	No joint effusion	71	5.24	0.819	3.49	0.984	< 0.001*	
	Meniscus tear	82	5.51	0.758	3.63	1.094	< 0.001*	-1.495 (0.138)
	No meniscus tear	40	5.13	0.966	3.53	0.847	< 0.001*	
	Cyst	82	5.39	0.782	3.70	0.856	< 0.001*	1.314 (0.191)
	No cyst	40	5.38	0.979	3.40	1.277	< 0.001*	
	BME	81	5.38	0.784	3.67	0.922	< 0.001*	0.993 (0.323)
	No BME	41	5.39	0.972	3.46	1.185	< 0.001*	
	ACL tear	33	5.36	0.742	3.82	1.044	< 0.001*	1.473 (0.143)
	No ACL tear	89	5.39	0.887	3.52	1.001	< 0.001*	

* Paired t test; $p < 0.001$.
† Wilcoxon signed rank test; $p < 0.001$.
‡ Wilcoxon signed rank test; $p < 0.01$.
§ One-way ANOVA test; $p < 0.01$.
‖ Student t test; $p < 0.01$.
ACL, anterior cruciate ligament; BME, bone marrow edema; BMI, body mass index; CVD, cardiovascular disease; MSD, musculoskeletal disease; N/A, not applicable; NRS, numeric rating scale; OA, osteoarthritis.

Table 4. Comparison of WOMAC Scores Before and After Treatment.

		N	Admission		Discharge		Before & after	Between groups
			Mean	SD	Mean	SD	*p*	F(*p*)
Hospitalization period (d)	4-14	29	49.69	15.41	38.86	14.11	0.001†	1.879 (0.137)
	15-28	33	49.18	15.19	37.15	14.91	< 0.001*	
	29-42	37	53.68	14.43	33.08	14.93	< 0.001*	
	43-	23	52.74	18.66	38.61	14.53	0.011‡	
Sex	Male	17	53.65	9.28	34.35	13.33	< 0.001*	1.074 (0.285)
	Female	105	50.96	16.46	36.96	14.91	< 0.001*	
Age (y)	40-59	31	51.39	15.89	35.29	14.32	< 0.001*	0.663 (0.517)
	60-69	68	50.62	16.79	37.56	15.67	< 0.001*	
	70-	23	53.39	11.82	35.52	12.30	< 0.001*	
BMI	Normal & underweight	48	50.67	17.23	34.71	14.11	< 0.001*	0.163 (0.849)
	Pre-obese	31	48.81	13.23	35.13	15.95	< 0.001*	
	Obese Class 1 & 2	42	54.05	15.56	39.86	14.30	< 0.001*	
OA compartment	Medial	35	50.86	16.28	38.89	14.51	< 0.001*	
	Lateral	3	69.67	2.52	38.33	10.21	N/A	
	Patellofemoral	24	49.88	16.96	29.79	13.58	< 0.001*	
	Medial + lateral	2	36.00	31.11	30.00	8.49	N/A	
	Medial + patellofemoral	43	50.58	14.03	37.33	15.72	< 0.001*	
	Lateral + patellofemoral	1	71.00	N/A	53.00	N/A	N/A	
	Medial + lateral + patellofemoral	14	54.21	14.49	39.71	12.99	< 0.001*	
History	Hypertension	35	52.77	17.21	37.8	14.63	< 0.001*	-0.086 (0.931)
	No hypertension	87	50.76	15.06	36.11	14.75	< 0.001*	
	CVD	26	56.5	12.41	37.04	14.31	< 0.001*	-1.446 (0.151)
	No CVD	96	49.94	16.20	36.48	14.85	< 0.001*	
	MSD	90	51.33	15.70	37.41	14.93	< 0.001*	0.800 (0.425)
	No MSD	32	51.34	15.79	34.31	13.92	< 0.001*	
Comorbidities with OA	Joint effusion	51	51.73	16.03	35.55	14.23	< 0.001*	-0.713 (0.477)
	No joint effusion	71	51.06	15.49	37.35	15.05	< 0.001*	
	Meniscus tear	82	54	14.01	37.37	13.96	< 0.001*	-1.600 (0.112)
	No meniscus tear	40	45.88	17.54	35.03	16.12	0.003†	
	Cyst	82	52.15	13.96	35.57	13.58	< 0.001*	-1.548 (0.124)
	No cyst	40	49.68	18.75	38.70	16.68	< 0.001*	
	BME	81	52.36	14.08	35.83	14.14	< 0.001*	-1.483 (0.141)
	No BME	41	49.32	18.41	38.12	15.76	< 0.001*	
	ACL tear	33	56.42	12.59	39.06	15.75	< 0.001*	-0.936 (0.351)
	No ACL tear	89	49.45	16.32	35.69	14.24	< 0.001*	

* Paired t test; $p < 0.001$.
† Paired t test; $p < 0.01$.
‡ Paired t test; $p < 0.05$.
ACL, anterior cruciate ligament; BME, bone marrow edema; BMI, body mass index; CVD, cardiovascular disease; MSD, musculoskeletal disease; N/A, not applicable; NRS, numeric rating scale; OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 5. Comparison of EQ-5D-5L Scores Before and After Treatment.

		N	Admission		Discharge		Before & after	Between groups
			Mean	SD	Mean	SD	*p*	F (*p*)
Hospitalization period (d)	4-14	29	0.64	0.154	0.67	0.249	0.141	0.481 (0.696)
	15-28	33	0.57	0.170	0.59	0.278	0.567	
	29-42	37	0.54	0.140	0.62	0.225	0.026‡	
	43-	23	0.56	0.224	0.62	0.199	0.275	
Sex	Male	17	0.54	0.154	0.68	0.248	0.029‡	-1.889 (0.061)
	Female	105	0.58	0.174	0.61	0.239	0.128	
Age (y)	40-59	31	0.57	0.169	0.66	0.199	0.052	0.567 (0.569)
	60-69	68	0.57	0.186	0.61	0.248	0.181	
	70-	23	0.59	0.134	0.62	0.276	0.494	
BMI	Normal & underweight	48	0.58	0.165	0.58	0.280	0.861	1.386 (0.254)
	Pre-obese	31	0.60	0.185	0.69	0.233	0.064	
	Obese Class 1 & 2	42	0.55	0.169	0.62	0.190	0.019‡	
OA compartment	Medial	35	0.57	0.158	0.66	0.238	0.037‡	
	Lateral	3	0.54	0.208	0.61	0.185	N/A	
	Patellofemoral	24	0.59	0.153	0.66	0.203	0.058	
	Medial + lateral	2	0.57	0.207	0.54	0.326	N/A	
	Medial + patellofemoral	43	0.58	0.192	0.62	0.226	0.350	
	Lateral + patellofemoral	1	0.356	N/A	0.72	N/A	N/A	
	Medial + lateral + patellofemoral	14	0.55	0.184	0.51	0.343	0.528	
History	Hypertension	35	0.55	0.173	0.55	0.303	0.967	-1.566 (0.120)
	No hypertension	87	0.58	0.171	0.65	0.205	0.030‡	
	CVD	26	0.52	0.178	0.54	0.290	0.783	-0.743 (0.462)
	No CVD	96	0.59	0.168	0.65	0.221	0.010‡	
	MSD	90	0.56	0.179	0.60	0.250	0.171	-1.135 (0.259)
	No MSD	32	0.60	0.150	0.69	0.199	0.013‡	
Comorbidities with OA	Joint effusion	51	0.56	0.167	0.64	0.191	0.012‡	1.058 (0.292)
	No joint effusion	71	0.58	0.176	0.61	0.271	0.299	
	Meniscus tear	82	0.57	0.165	0.62	0.254	0.078	-0.078 (0.938)
	No meniscus tear	40	0.59	0.186	0.64	0.212	0.112	
	Cyst	82	0.58	0.171	0.61	0.220	0.204	-1.226 (0.222)
	No cyst	40	0.56	0.174	0.65	0.280	0.032‡	
	BME	81	0.56	0.177	0.61	0.249	0.052	0.234 (0.815)
	No BME	41	0.61	0.156	0.65	0.224	0.204	
	ACL tear	33	0.55	0.139	0.58	0.240	0.414	-0.456 (0.649)
	No ACL tear	89	0.58	0.182	0.64	0.240	0.026‡	

* Paired t test; $p < 0.001$.
† Paired t test; $p < 0.01$.
‡ Paired t test; $p < 0.05$.
ACL, anterior cruciate ligament; BME, bone marrow edema; BMI, body mass index; CVD, cardiovascular disease; EQ-5D-5L, 5-level EuroQol- 5 Dimension; MSD, musculoskeletal disease; N/A, not applicable; NRS, numeric rating scale; OA, osteoarthritis.

Table 6. Comparing Improvement of Indicators Between Patients with OA in the Medial and with OA in the Patellofemoral Compartments.

Indicators (admission-discharge)	Medial (n = 34) Mean (SD)	Patellofemoral (n = 24) Mean (SD)	t	p
NRS	1.71 (1.000)	2.13 (1.361)	-1.35226	0.182
WOMAC (pain)	2.24 (3.411)	4.42 (4.074)	-2.21235	0.031*
WOMAC (stiffness)	0.65 (1.921)	1.67 (1.736)	-2.07029	0.043*
WOMAC (function)	8.76 (14.033)	14.00 (14.213)	-1.39201	0.169
WOMAC (total)	11.65 (18.299)	20.08 (18.928)	-1.70496	0.094
EQ-5D-5L	-0.09 (0.239)	-0.07 (0.166)	-0.39934	0.691

*Student t test; $p < 0.05$.
EQ-5D-5L, 5-level EuroQol- 5 Dimension; NRS, numeric rating scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 7. Comparing Improvement of Indicators in Patients with and Without OA in the Medial Compartment.

Indicators (admission-discharge)	Without medial (n = 29) Mean (SD)	With medial (n = 93) Mean (SD)	t	p
NRS	2.14 (1.382)	1.68 (0.991)	1.978	0.5
WOMAC (pain)	4.66 (3.754)	2.23 (3.885)	2.963	0.004*
WOMAC (stiffness)	1.76 (1.640)	0.85 (2.090)	2.144	0.034†
WOMAC (function)	14.86 (13.603)	9.62 (14.033)	1.768	0.08
WOMAC (total)	21.28 (17.840)	12.70 (18.798)	2.171	0.032†
EQ-5D-5L	-0.0760 (0.18393)	-0.0418 (0.24678)	-0.689	0.492

*Student t test; $p < 0.01$.
†Student t test; $p < 0.05$.
EQ-5D-5L, 5-level EuroQol- 5 Dimension; NRS, numeric rating scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

in Table 5 were grouped by hospitalization period with only 1 hospitalization period (29-42 days) which improved significantly ($p < 0.05$). When grouped by BMI score, only the obese Class 1 and 2 showed significant improvement ($p < 0.05$). When grouped by knee compartment, only the medial group improved significantly ($p < 0.05$). When comparing groups of patients according to hypertension, cardiovascular disease, and musculoskeletal disease, the group without each condition/disease showed significant improvement ($p < 0.05$). When grouped by comorbidities, the group of patients with joint effusion, without a cyst, or without ACL tears showed significant improvement ($p < 0.05$).

When comparing the improvement of indicators between patients with OA in the medial compartments and those with OA in the patellofemoral compartments, there were significant differences in the WOMAC (pain, stiffness) scores ($p < 0.05$) (Table 6). When comparing improvement of indicators of the 122 inpatients both with and without OA in the medial compartment, there were significant differences in WOMAC (pain, stiffness, total) scores ($p < 0.05$) (Table 7). A comparison of the improvement of indicators between those patients with and without OA in the lateral compartment, showed no significant differences (Table 8). Similarly, when comparing the improvement of indicators in patients with and without OA in the patellofemoral compartment, there were no significant differences in the indicators (Table 9).

Discussion

In this study, a total of 122 inpatients who were admitted to the Hospital of Korean Medicine for knee pain, and were diagnosed with knee OA based on MRI findings, underwent Korean medicine

Table 8. Comparing Improvement of Indicators Between Patients with and Without OA in the Lateral Compartment.

Indicators (admission-discharge)	Without lateral (n = 102) Mean (SD)	With lateral (n = 20) Mean (SD)	t	p
NRS	1.76 (1.127)	1.90 (1.021)	-0.498	0.619
WOMAC (pain)	2.77 (4.162)	2.95 (2.929)	-0.18	0.858
WOMAC (stiffness)	0.94 (2.082)	1.70 (1.593)	-1.542	0.126
WOMAC (function)	10.71 (14.737)	11.70 (10.142)	-0.288	0.774
WOMAC (total)	14.42 (19.824)	16.35 (13.164)	-0.545	0.589
EQ-5D-5L	-0.0609 (0.22745)	0.0062 (0.25912)	-1.179	0.241

EQ-5D-5L, 5-level EuroQol- 5 Dimension; NRS, numeric rating scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 9. Comparing Improvement of Indicators Between Patients with And Without OA in the Patellofemoral Compartment.

Indicators (admission-discharge)	Without patellofemoral (n = 40) Mean (SD)	With patellofemoral (n = 82) Mean (SD)	t	p
NRS	1.65 (0.949)	1.85 (1.177)	-0.953	0.343
WOMAC (pain)	2.50 (3.389)	2.95 (4.245)	-0.587	0.558
WOMAC (stiffness)	0.9 (1.892)	1.15 (2.091)	-0.63	0.53
WOMAC (function)	9.73 (14.160)	11.43 (14.058)	-0.626	0.532
WOMAC (total)	13.13 (18.363)	15.52 (19.162)	-0.658	0.512
EQ-5D-5L	-0.0791 (0.23508)	-0.0356 (0.23227)	-0.966	0.336

EQ-5D-5L, 5-level EuroQol- 5 Dimension; NRS, numeric rating scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

treatment. Seventeen males and 105 females were included in this study (ratio of 1:6.17). Having more females with knee OA was consistent with another study of knee OA [29]. The age distribution of the patients included in this study, all of whom underwent Korean medicine treatment, were mostly in their 60s. A cause of knee OA included trauma, however, the cause was unknown in most cases. This is consistent with the finding that knee OA is caused by degeneration [29]. Only one of the 122 patients were within the underweight BMI category. Approximately 38.52% patients had a BMI in the normal range, whereas most had a BMI in the pre-obese category or higher (59.84%). This finding supports the results of a previous study on the correlation between obesity and OA [15]. The high rate of hypertension and cardiovascular disease may be due to the increased frequency of these 2 conditions/diseases in those patients with a high BMI.

In this study, the MRI findings suggested that knee OA mostly manifests in the medial and patellofemoral compartments, and there were many cases of coexistence in both compartments. Furthermore, 118 (96.72%) patients had primary knee OA based on MRI findings. Since the phenotype was determined based only on MRI findings, there was a limitation in assessing whether the disease developed secondary to another disease. In the current study, the distribution of comorbidities on MRI findings was assessed. Meniscus tears, cysts, and bone marrow edema were frequently observed. This finding is consistent with the results of previous studies on common complications of knee OA [12,13,15].

The participants underwent Korean medicine treatment including acupuncture, cupping, pharmacopuncture, herbal medicine, chuna therapy, and medicinal steaming therapy, as well as Western treatments such as manual therapy, and ESWT. Acupuncture is included in the OA treatment guidelines using Korean medicine owing to its beneficial effects and low risk [30]. Various clinical trials and meta-analyses have demonstrated that acupuncture [31-36], and electroacupuncture (where an electric current is passed through a needle, has been shown to be effective for knee OA [37]. Additionally, a systematic review and meta-analysis study has shown that combination therapy of Western medicine and cupping therapy leads to greater treatment efficacy

Table 10. Baseline Characteristics of Patients with Knee OA (n = 122).

	N (%)
Sex	
Male	17 (13.9)
Female	105 (86.1)
Age (y)	
40-49	3 (2.46)
50-59	28 (22.95)
60-69	68 (55.74)
70-79	20 (16.39)
80-	3 (2.46)
Cause	
Reason unknown	93 (76.23)
Fall / trauma	16 (13.11)
Overwork or over exercise	12 (9.84)
Surgery	1 (0.82)
BMI (kg/m2)	
Underweight (0<, <18.5)	1 (0.82)
Normal (18.5≤, <23)	47 (38.52)
Pre-obese (23≤, <25)	31 (25.41)
Obese Class I (25≤, <30)	37 (30.33)
Obese Class II (30≤, <35)	5 (4.10)
Missing value	1 (0.82)
History*	
Musculoskeletal disease	90 (73.77)
Hypertension	35 (28.70)
ardiovascular disease	26 (21.31)
Gastrointestinal disease	16 (13.11)
Respiratory disease	8 (6.56)
Diabetes mellitus	8 (6.56)
Depression disorder	1 (0.82)

Table 10. (Continued).

	N (%)
OA compartment	
Medial	35 (28.69)
Lateral	3 (2.46)
Patellofemoral	24 (19.67)
Medial + lateral	2 (1.64)
Medial + patellofemoral	43 (35.25)
Lateral + patellofemoral	1 (0.82)
Medial + lateral + patellofemoral	14 (11.48)
OA phenotype	
Primary	118 (96.72)
Secondary	4 (3.28)
Comorbidity*	
Meniscus tear	82 (67.21)
Yst	82 (67.21)
Bone marrow edema	81 (66.39)
Fluid	51 (41.80)
ACL Tear	33 (27.05)
Chondral lesion (Grade 1)	9 (7.38)
Hospitalization period (d)	
4-7	11 (9.02)
8-14	18 (14.75)
15-21	15 (12.30)
22-28	18 (14.75)
29-35	19 (15.57)
36-42	18 (14.75)
43-49	13 (10.66)
50-	10 (8.20)

* Multiple check.
ACL, anterior cruciate ligament; BMI, body mass index; OA, osteoarthritis.

Table 11. Number of Treatment Times.

Treatments	Mean*	SD*	Max
Acupuncture	40.24	23.03	98
Cupping	41.58	28.02	126
Pharmacopunture	41.62	29.55	137
Herbal medicine (d)	27.38	16.41	76
Chuna therapy	21.16	16.41	73
Medicinal steaming therapy	17.42	20.80	114
Manual therapy	14.48	10.64	50
ESWT	4.63	6.49	22

*Values for mean and SD are expressed in number of times unless otherwise stated.
ESWT, extracorporeal shock wave therapy.

Table 12. Distribution of Treatments Times.

No. of times	Acupuncture		Cupping		Pharmaco -puncture		Herbal medicine (d)*		Chuna therapy		Medicinal steaming therapy		Manual therapy		ESWT	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
0	1	0.82	2	1.64	6	4.92	2	1.64	15	12.30	35	28.69	10	8.20	66	54.10
1–10	9	7.38	11	9.02	16	13.11	20	16.39	23	18.85	25	20.49	38	31.15	28	22.95
11–20	23	18.85	24	19.67	11	9.02	23	18.85	27	22.13	17	13.93	36	29.51	23	18.85
21–30	10	8.20	13	10.66	16	13.11	26	21.31	26	21.31	18	14.75	33	27.05	5	4.10
31–40	20	16.39	15	12.30	16	13.11	23	18.85	16	13.11	16	13.11	2	1.64		
41–50	21	17.21	17	13.93	13	10.66	20	16.39	8	6.56	5	4.10	3	2.46		
51–60	17	13.93	16	13.11	16	13.11	2	1.64	4	3.28	3	2.46				
61–70	6	4.92	5	4.10	8	6.56	5	4.10	2	1.64	0	0.00				
71–80	8	6.56	6	4.92	7	5.74	1	0.82	1	0.82	0	0.00				
81–90	7	5.74	13	10.66	13	10.66			0	0.00	3	2.46				
Total	122	100	122	100	122	100	122	100	122	100	122	100	122	100	122	100

*Herbal medicine values are expressed in number of days.
ESWT, extracorporeal shockwave therapy.

and physical function in patients with knee OA compared with Western medicine alone [38]. Pharmacopuncture is a treatment in Korean medicine where herbal medicine extracts are injected at acupuncture points related to conditions/diseases, tender points, or positive reaction points based on meridian theory [39]. Studies have shown that various types of pharmacopuncture are effective for knee OA [40-42], and both acupuncture and pharmacopuncture do not cause serious side effects in musculoskeletal diseases [43]. In this study, Shinbaro pharmacopuncture was performed, which has been reported to have a similar efficacy and safety profile to celecoxib, a COX-2 inhibitor [44]. Clinical studies have also demonstrated that herbal medicine is effective in the treatment of knee OA [45-47]. Chuna therapy is a representative Korean medicine treatment that treats an unbalanced body and a blocked meridian system using direct manual treatment. It is often used to treat spinal, joint, muscle-related, and viscerogenic conditions/

Table 13. Correlation Analysis Between Treatments and NRS Change.

	Acupuncture	Cupping	Pharmaco -puncture	Herbal medicine	Chuna therapy	Medicinal steaming therapy	Manual therapy	ESWT
Correlation coefficient	0.319	0.231	0.27	0.298	0.275	0.308	0.192	-0.025
p	< 0.001*	0.011‡	0.003†	< 0.001*	0.002†	0.001†	0.034‡	0.786

* Spearman correlation analysis; $p < 0.001$.
† $p < 0.01$.
‡ $p < 0.05$.
ESWT, extracorporeal shockwave therapy; NRS, numeric rating scale.

Table 14. Comparison of NRS, WOMAC, and EQ-5D-5L Scores Before and After Treatment.

	N	Admission		Discharge		*p*
		Mean	SD	Mean	SD	
NRS	122	5.39	0.847	3.60	1.018	< 0.001*
WOMAC (pain)	122	10.22	3.555	7.42	3.136	< 0.001*
WOMAC (stiffness)	122	4.09	1.676	3.02	1.535	< 0.001*
WOMAC (function)	122	37.02	11.427	26.16	10.833	< 0.001*
WOMAC (total)	122	51.34	15.659	36.60	14.676	< 0.001*
EQ-5D-5L	122	0.57	0.171	0.62	0.021	0.02†

* Paired t test; $p < 0.001$.
† Paired t test; $p < 0.05$.
EQ-5D-5L, 5-level EuroQol- 5 Dimension; NRS, numeric rating scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

diseases. Chuna therapy has been reported to improve flexor and extensor muscular tension in patients with OA [48].

Analysis of the correlation between treatment and indicator of pain improvement showed that the NRS score significantly correlated with all treatments except for ESWT. In particular, compared with the other treatments in this study, acupuncture, herbal medicine, and medicinal steaming therapy had a relatively higher correlation with NRS scores. Although the scores in this study were not high, these findings suggest that these 3 treatments played a major role in the Korean medicine treatment of knee OA when compared with the other treatments.

By comparing the NRS and WOMAC scores before and after treatment, Korean medicine treatment effectively controlled pain, stiffness, and physical function of the knee, regardless of sex, age, BMI, presence or absence of medical history, and presence or absence of comorbidities. Patients with a history of musculoskeletal disease showed less improvement in the NRS score compared with those patients without musculoskeletal disease. This indicated that patients with OA and musculoskeletal disease showed less improvement in pain after Korean medicine treatment than patients without a musculoskeletal disease. When grouped by compartment, the mean scores of all groups improved. In the group where analysis was possible, patients with medial and patellofemoral alone, patients with medial and lateral at the same time, and patients with OA in all 3 compartments showed significant improvement in NRS and WOMAC scores. It appears that Korean medicine treatment was effective in controlling knee pain, stiffness, and physical function in patients with OA in the aforementioned compartment.

When comparing EQ-5D-5L before and after treatment, the mean score showed significant improvement. This indicated that Korean medicine treatment was effective at improving the QoL of patients with OA. However, in subgroup analysis, not all groups were statistically significant. From the perspective of improving the QoL, when looking at subgroups of patients in terms of the hospitalization period, 4-6 weeks of Korean medicine treatment was the most suitable time period for improving QoL. By comparing the BMI groups, the higher the obesity index, the greater the likelihood that Korean medicine treatment could improve QoL. When looking at the subgroups in terms of the OA compartment, Korean medicine treatment was more effective in the medial compartment OA compared with other compartments in terms of improving QoL.

Korean medicine treatment was more effective in the patellofemoral compartment compared with the medial compartment in terms of pain and stiffness. Accordingly, Korean medicine treatment was more effective in patients without OA in the medial compartment compared with patients with OA in the

medial compartment in terms of pain and stiffness.

This was a retrospective study where a control group for comparison with the treatment group was not included. The lack of long-term follow-up also limited the assessment of the long-term effects of Korean medicine treatment. The participants in this study could have had diseases other than OA in their knee, therefore pain experienced in these patients may have been attributable to other conditions/diseases. Additionally, the MRI findings alone where not sufficient to provide the grade of OA, and consequently the number and type of Korean medicine treatment differed for each patient. Thus, the detailed effects of each treatment could not be evaluated. In the compartment group, since the number of patients in the lateral, medial + lateral, lateral + patellofemoral compartment was too small, statistical analysis could not be performed.

The current study was a relatively large-scale analysis study compared with previous studies which have analyzed the effects of Korean medicine treatment in inpatients. This study included a larger sample size for the analysis, which supports the results of previous studies. Quantitative indicators such as the NRS, WOMAC, and EQ-5D-5L scores were analyzed to objectively assess the effects of treatment. In particular, the detailed indicators of the WOMAC index were analyzed to evaluate improvements in the levels of pain, stiffness, and physical function. The patients included in this study had been diagnosed with OA based on the MRI findings. Thus, the comorbidities of soft tissues could be analyzed which allowed evaluation of the effects of Korean medicine treatment according to the OA compartment and comorbidities based on MRI findings.

Conclusion

Overall, Korean medicine treatment significantly reduced pain, stiffness, and physical dysfunction, and improved the QoL of patients with knee OA, suggesting that it may be an effective alternative to the current conservative treatments.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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