TABLE 3. Multivariate Analysis for Delayed Recovery

Factors	*P*	Odds Ratio (95% CI)
Age	0.085	1.08 (0.99-1.17)
Sex	0.374	0.45 (0.08-2.62)
Duration of symptom	0.554	0.98 (0.92-1.04)
Type of HNP	0.049	5.17 (0.03-0.99)
Percent occupancy of HNP	0.233	6.58 (0.98-1.12)
Migration of HNP	0.871	1.20 (0.13-11.1)
Severity of motor weakness	0.019	19.6 (0.004-0.61)

CI indicates confidence interval; HNP, herniated nucleus pulposus.

require surgery, and some authors have reported that 70% to 90% of the patients with LDH respond to conservative therapy.[9–11] The main indications for surgery are severe and persistent leg pain, persistent paresis, such as motor deficit, and bladder-bowel dysfunction. In particular, spinal surgeons tend to recommend surgery for LDH patients with motor deficit, but there are few reports regarding the risk factors for motor weakness caused by LDH and residual motor weakness after surgery. Weakness of TA muscle, referred to as foot-drop, is most often seen in patients with LDH at L4/5 level.[12,13] On the basis of these aspects, we focused on the muscle weakness of TA in the patients with LDH at L4/5 level, and analyzed their clinical outcomes and risk factors for motor deficit. One limitation of our study may be that preoperative electromyography (EMG) was only undertaken in some of the patients, rather than all the patients. However, the clinical information obtained by MMT is not inferior to the one provided by electromyography, as long as the muscle strength is assessed using standard maneuvers.

In this study, 93% of the patients with motor deficit achieved complete recovery after surgery. Girardi et al[13] reported that 71% of the patients with foot drop fully recovered after surgery, whereas Aono et al[12] reported a rate of 61%. The rate of complete recovery in this study was much higher than that in earlier reports. We consider that this difference arises because the earlier studies included patients with lumbar spinal canal stenosis. Postacchini et al[5] reported that 76% of patients with motor deficit caused by LDH fully recovered after surgery. However, they made estimates of several muscles in patients with LDH at several levels, and their results cannot be simply compared with the present results.

The JOA score of patients with motor deficit at the final follow-up was the same as that of patients without motor deficit. However, patients with severe deficit required a longer time to achieve complete recovery or had incomplete recovery. All patients with mild muscle deficit (MMT4) recovered completely within the mean duration of 2.9 months, whereas 78.6% of patients with severe muscle weakness recovered completely within a mean duration of 9.5 months. Postacchini et al[5] reported an inverse relationship between the severity of preoperative motor deficit and the ability to recover completely. The present results also indicate that the severity of the preoperative motor deficit influenced the degree of recovery and the time required to achieve complete recovery for motor deficit caused by LDH. Therefore, the timing of surgical intervention seems to be very important for obtaining a satisfactory surgical outcome for patients with LDH.

Our multivariate logistic regression analysis showed that noncontained type and migrated HNP were the most important risk factors for motor deficit. Jonsson and Stromqvist[8] showed that pain and neurologic deficit were statistically more severe in patients the with noncontained type of HNP than in patients with contained type of HNP. Postacchini et al[5] and Dubourg et al[4] reported that extruded HNP was often associated with motor deficit, and our present results are consistent with their reports. Some researchers reported that infiltration of macrophages along the margins of extruded discs was detected in 80% to 100% of their cases.[14,15] Therefore, we speculate that these inflammatory responses may cause severe damage to the nerve root and motor deficit. Caudal or cranial migration of HNP is considered to be another risk factor for the occurrence of motor deficit. Takahashi et al[16] showed that the magnitude of nerve root pressure was correlated with the severity of neurologic deficits. We speculate that the nerve root is severely compressed between lateral recess and HNP when HNP migrated caudally. In contrast, cranial migration of HNP can cause injury to 2 nerve roots (such as L4 and L5 nerve roots), and this may cause motor deficit.

We also analyzed the risk factors for delayed recovery. Preoperative severe motor deficit (MMT$\leq$3) and noncontained type of HNP were identified as important risk factors for delayed recovery. Postacchini et al[5] also reported that patients with severe motor deficit required longer time for recovery than patients with mild motor deficit, and our results support their findings. Another important risk factor was the noncontained type of HNP. Several earlier reports have shown that transligamentous or sequestrated (noncontained) HNP spontaneously decrease in size. Komori et al[9] reported that extruded and migrated HNP tended to decrease or disappear, and that patients in whom HNP markedly decreased or disappeared showed good result in natural history. Ahn et al[17] reported that 79% of transligamentous herniation and 100% of sequestrated herniation reduced in size with an average follow-up of 6.8 months. These reports indicate that the noncontained type of HNP is associated with good prognosis without surgical intervention. However, this study suggests that patients with the noncontained type of HNP and motor deficit required a longer time to achieve complete recovery, and that did not always show good prognosis. This large difference is considered to arise from differences in patient populations. Specifically, all patients in the earlier study were treated without surgery, whereas all patients in this study underwent surgery. A prospective study is required to clarify the prognosis of patients with noncontained type of HNP.

Symptom duration before surgery was not a significant risk factor for delayed recovery in this study.

Postacchini et al[5] reported that patients with muscle weakness who underwent surgery at 3 months after the onset of muscle weakness did not achieve complete recovery. Aono et al[12] reported that the duration of motor deficit significantly affected surgical outcome. In this study, symptom duration was defined as the interval from onset of subjective neurologic symptoms to surgery, rather than onset of muscle weakness, because patients are often unaware of mild muscle weakness. This difference in the definitions of symptom duration may have affected the results in each study.

This study clearly indicated the important risk factors for motor deficit caused by LDH and delayed recovery after surgery. However, the fact that this study was retrospective, and the fact that we only analyzed patients with LDH who underwent surgery are limitations of this study. To clarify the best choice of treatment for patients with LDH and motor deficit, a prospective randomized study based on these results is required.

In conclusion, noncontained type and migrated HNP seem to be the most important risk factors for motor deficit in patients with LDH. In addition, severe motor deficit (MMT$\leq$3) and noncontained type of HNP seem to be important risk factors for delayed recovery. For patients with these factors, care should be taken to prevent deterioration of their motor function, because the severity of motor deficit affects the degree of recovery and the time required to achieve complete recovery after surgery.

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The influence of approach side on facet preservation in microscopic bilateral decompression via a unilateral approach for degenerative lumbar scoliosis

Clinical article

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Object. The authors compared the clinical outcomes of microscopic bilateral decompression via a unilateral approach (MBDU) for the treatment of degenerative lumbar scoliosis (DLS) and for lumbar canal stenosis (LCS) without instability. The authors also compared postoperative spinal instability in terms of different approach sides (concave or convex) following the procedure.

Methods. The authors retrospectively reviewed data obtained in 50 consecutive patients (25 in the DLS group and 25 in the LCS group) who underwent MBDU; the minimum follow-up period was 2 years. Patients with DLS were divided into 2 subgroups according to the surgical approach side: a concave group (23 segment) and a convex group (17 segments). The Japanese Orthopaedic Association Scale scores for the assessment of low-back pain were evaluated before surgery and at final follow-up. The Japanese Orthopaedic Association Scale scores and recovery rates were compared between the DLS and LCS groups, and between the convex and concave groups. Cobb angle and scoliotic wedging angle (SWA) were evaluated on standing radiographs before surgery and at final follow-up. Facet joint preservation (the percentage of preservation) was assessed on pre- and postoperative CT scans, compared between the LCS and DLS groups, and compared between the concave and convex groups. The influence of approach side on postoperative progression of segmental instability was also examined in the DLS group.

Results. The mean recovery rate was 58.7% in the DLS and 62.0% in the LCS group. The mean recovery rate was 58.6% in the convex group and 60.6% in the concave group. There were no significant differences in recovery rates between the LCS and DLS groups, or between the DLS subgroups. The mean Cobb angles in the DLS group were significantly increased from 12.7° preoperatively to 14.1° postoperatively ($p < 0.05$), and mean preoperative SWAs increased significantly from 6.2° at L3–4 and 4.1° at L4–5 preoperatively to 7.4° and 4.9°, respectively, at final follow-up ($p < 0.05$). There was no significant difference in percentage of preservation between the DLS and LCS groups. The mean percentages of preservation on the approach side in the DLS group at L3–4 and L4–5 were 89.0% and 83.1% in the convex group, and those in the concave group were 67.3% and 77.6%, respectively. The percentage of preservation at L3–4 was significantly higher in the convex than the concave group. The mean SWA had increased in the concave group ($p = 0.01$) but not the convex group ($p = 0.15$) at final follow-up.

Conclusions. The MBDU can reduce postoperative segmental spinal instability and achieve good postoperative clinical outcomes in patients with DLS. The convex approach provides surgeons with good visibility and improves preservation of facet joints. *(DOI: 10.3171/2010.5.SPINE091001)*

Key Words • microscopic decompression • unilateral approach • degenerative lumbar scoliosis • facet joint preservation • postoperative instability

Lumbar spinal canal stenosis combined with scoliosis is often seen in elderly patients. The patients suffer from low-back pain, radiating leg pain, and intermittent claudication. Conservative therapy may not be adequate, and some form of surgical intervention is generally indicated. The choice of surgical method depends on the magnitude of the curvature, spinal instability, and the symptoms. Simmons[18] classified 2 types of adult scoliosis, depending on the presence or absence of preexisting scoliosis. Aebi[2] classified 4 types scoliosis based on the origin. These 2 authors recommended corrective surgery for degenerative adult scoliosis when

Abbreviations used in this paper: AP = anteroposterior; DLS = degenerative lumbar scoliosis; JOA = Japanese Orthopaedic Association; LCS = lumbar spinal canal stenosis; MBDU = microscopic bilateral decompression via a unilateral approach; SWA = scoliotic wedging angle.

the disease was idiopathic and decompression and fusion surgery when the scoliosis was degenerative (de novo) in nature.[2,18] The surgical aims differ between these 2 types of scoliosis: corrective surgery aims to improve spinal balance, whereas decompression and short fusion aims to relieve neurological symptoms. However, the indications for surgery and definition of the fusion area have not been established. In addition, DLS is seen predominantly in the elderly population, and elderly patients usually have more medical comorbidities, such as hypertension, diabetes, and cardiopulmonary disease.[14] Furthermore, osteoporosis in the elderly makes spinal implants difficult to anchor, even with a pedicle screw fixation system.[2,4] Patients with DLS usually require long-segment fusion, which can increase the risk instrumentation-related complications. Surgery for degenerative adult scoliosis can result in significant complications, including pseudarthrosis, adjacent-segment disease, neurological deficits, cardiopulmonary disease, deep vein thrombosis, and wound infection. The incidence of complications reported in most series has been high, ranging from 20% to 80%.[2,3]

Preservation of the posterior elements is the most important factor in the success of decompression surgery for LCS.[1,5,10,17] Decompressive laminectomy is one of the most common surgical procedures for LCS, and some authors have reported good clinical outcomes after laminectomy.[7,21] However, despite affording a wide decompression, laminectomy or "unroofing" of the spinal canal, can cause destruction or impairment insufficiency of the pars interarticularis or facet joints, resulting in segmental instability and paravertebral muscle atrophy.[3,17] Some authors have recently reported good clinical outcomes following minimally invasive decompression in which the posterior elements, such as the paravertebral muscle, facet joints, and lamina, have been preserved.[6,8,19] Good clinical outcomes in patients with LCS have also been reported for MBDU, which was initially described by Young et al.[23] in 1988 and was later modified by Weiner et al.[20] Additionally, a few authors have reported the clinical results of MBDU for LCS in cases involving mild instability, such as spondylolisthesis[15] and hemodialysis.[16] However, there have been few reports regarding the clinical outcome after decompression for DLS. We initiated the use of the MBDU for DLS in an attempt to reduce postoperative instability. In the present study we compared the clinical outcomes of MBDU for DLS and for LCS without instability. The postoperative instability following concave- or convex-side approaches during MBDU for DLS were also compared.

Methods

The authors retrospectively reviewed data obtained in 50 consecutive patients with LCS who underwent MBDU; the minimum follow-up period was 2 years. The patients were divided into 2 groups, according to the nature of the spinal deformity: 25 patients with DLS group and and 25 patients with LCS without spinal deformity. The mean age in the DLS group was 69.6 years (range 53–82 years), and there were 10 men and 15 women; the mean age in the LCS group was 70.1 years (range 54–84 years), and there were 15 men and 10 women. The mean follow-up duration 43.6 months (range 24–89 months) in the DLS group and 42.1 months (range 24–79 months) in the LCS group. There were no significant intergroup differences in terms of the aforementioned parameters ($p > 0.05$). Decompression was performed at a single level in 10 cases in the DLS group and 6 cases in the LCS group; at 2 levels in 10 in the DLS group and in 11 cases in the LCS group, and at 3 levels in 5 cases in the DLS group and in 6 cases in the LCS group. Demographic and disease-related data are summarized in Table 1. Surgery was performed at L3–4 (18 segments), L4–5 (22 segments), and at other levels (5 segments) in the DLS group, and at L3–4 (16 segments), L4–5 (23 segments), and at other levels (11 segments) in the LCS group. We radiographically evaluated the L3–4 and L4–5 levels in both groups (40 in the DLS group and 39 in the LCS group [having excluding "other levels" from the analysis of both groups]). We divided the decompression levels in the DLS group into 2 subgroups according to the approach side of the surgery: from the concave side (23 segments) and from the convex side (17 segments). Details of the decompression segments are shown in Table 2. The following clinical and radiographic records were available for all patients: medical charts, standing AP and lateral radiographs obtained preoperatively and at least 2 years after surgery, and preoperative and postoperative CT scans.

Surgical Decision Making

Patients in whom the Cobb angle exceeded 10° in the coronal plane were considered to have DLS. Curvatures in all patients were classified as de novo scoliosis. Patients with spondylolisthesis and spondylolysis were excluded from the LCS group. Patients from both groups with neurogenic intermittent claudication (radiculopathy or cauda equina syndrome), and with no response to conservative therapy over at least 3 months, were considered to be suitable to undergo MBDU. Lumbar canal stenosis was confirmed by MR imaging, myelography, and CT myelography. Exclusion criteria for MBDU in patients with DLS were as follows: 1) Cobb angle greater than 25°, 2) severe low-back pain, 3) changes in segmental disc wedging between standing and prone position greater

TABLE 1: Summary of demographic and disease-related data

Characteristic	DLS Group	LCS Group	p Value
no. of patients	25	25	
male/female ratio	10:15	15:10	0.041
age (yrs)			
mean	69.6	70.1	0.82
range	53–82	54–84	
follow-up (mos)			
mean	43.6	42.1	0.76
range	24–89	24–79	
no. of decompression levels			0.17
1	10	6	
2	10	11	
3	5	6	
total	45	50	

TABLE 2: Decompression segments in 2 groups*

Variable	DLS Group	LCS Group	p Value
decompression level			0.17
L3–4†	18	16	
L4–5†	22	23	
others	5	11	
approach side‡			
concave	23	NA	
convex	17	NA	

* NA = not applicable.

† Radiographic data were only evaluated at the L3–4 and L4–5 segments in each group.

‡ The DLS group was divided into 2 subgroups, according to the approach side at surgery.

than 5°, 4) lateral disc slippage greater than 3 mm, and 5) foraminal stenosis needing more than 50% facetectomy for decompression.

Surgical Procedures

An approximately 35-mm midline incision for 1-level decompression (for example, at L4–5) was made to unilaterally expose the posterior elements lateral to the facet joints. Using a high-speed drill (with a 3- or 4-mm diamond-tipped bur) and a microscope, we removed the L-4 lamina cranially to the attachment of the ligamentum flavum, only minimally resecting the medial part of the L4–5 facet joint. The L-5 lamina was removed caudally to the attachment of the ligamentum flavum. Using a Kerrison rongeur and microcurette, the medial, cranial, and caudal margins of the ligamentum flavum were freed. The contralateral side was then approached. With the operating table rotated approximately 25° degree to the contralateral side, the L-4 spinous process was undercut, and the deeper portion of the interspinous ligament was removed to visualize the posterior surface of the contralateral ligamentum flavum. The caudal portion of the L-4 inner lamina and cranial part of the L-5 inner lamina were then partially removed using a high-speed drill to expose the whole ligamentum flavum. The contralateral facet was trimmed using the high-speed drill, and the attachment of the facet portion of the ligamentum flavum was detached using a microcurette or Kerrison rongeur. Finally, the ligamentum flavum was removed in 1 or 2 pieces. Decompression of the bilateral nerve roots was then evaluated.

Clinical Evaluation

The JOA score for assessment of low-back pain was evaluated before surgery and at final follow-up. The JOA score comprises 9 points assigned for subjective symptoms, 6 points for clinical signs, and 14 points for the restriction of activities of daily living, giving a total score of 29 points (Table 3).[22] The recovery rate was calculated as follows: (postoperative JOA score – preoperative JOA score)/(29 – preoperative JOA score) × 100(%).[3] We compared the JOA Scale scores and recovery rates between the DLS and LCS groups, as well as between the convex and concave groups.

Radiographic Evaluation

The Cobb angle and SWA were evaluated radiographically on standing radiographs before surgery and at final follow-up (Fig. 1). Facet joint preservation was evaluated on CT scans. The length of the facet joint was measured using Scion Image software, and the percentage of facet preservation was calculated using the equation: percentage of preserved facet = the length of the postoperative facet (b)/the length of the preoperative facet (a) × 100 (Fig. 2). The percentage of preserved facet was compared between the LCS and DLS groups, as well as between the concave and convex groups. We also analyzed the influence of the approach side on postoperative progression of segmental instability in the DLS group.

Statistical Analysis

All data were analyzed statistically using the ANOVA, Mann-Whitney U-test, paired t-test, or unpaired t-test, as

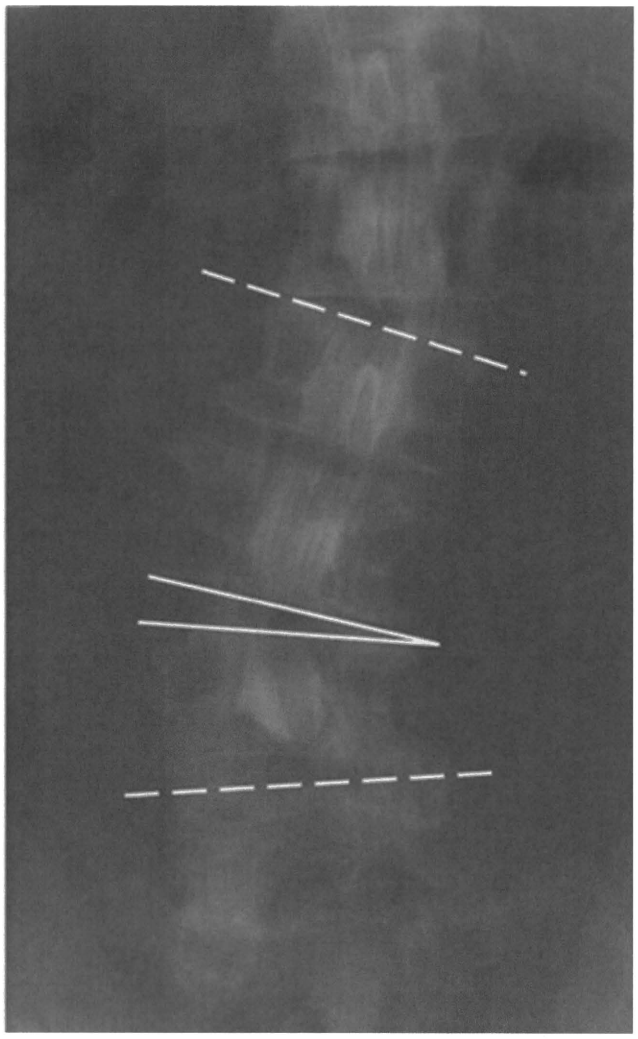

Fig. 1. Radiographic parameters. *Dotted lines* indicate Cobb angle and *solid lines* indicate scoliotic wedging angle.

TABLE 3: Summary of the JOA scoring system for treatment of low-back pain*

Factor	Item	Description	Score
subjective symptoms	low-back pain (3 points)	none	3
		occasional mild pain	2
		frequent mild or occasional severe pain	1
		continuous severe pain	0
	leg pain &/or tingling (3 points)	none	3
		occasional mild symptoms	2
		frequent mild or occasional severe symptoms	1
		continuous severe symptoms	0
	gait (3 points)	normal	3
		able to walk farther than 500 m although results in pain, tingling, &/or muscle weakness	2
		unable to walk farther than 500 m, results in pain, tingling, &/or muscle weakness	1
		unable to walk farther than 100 m, results in pain, tingling, &/or muscle weakness	0
objective symptoms	straight leg–raising test (2 points)	normal	2
		30–70°	1
		<30°	0
	sensory abnormality (2 points)	normal	2
		mild disturbance (not subjective)	1
		marked disturbance	0
	motor disturbance (MMT) (2 points)	normal (Grade 5)	2
		slight weakness (Grade 4)	1
		marked weakness (Grade 3–0)	0
restriction of ADLs (14 points)	turning over while lying standing washing leaning forward sitting (about 1 hr) lifting or holding heavy objects walking	no restriction moderate restriction severe restriction	2 1 0
urinary bladder function (−6 points)		normal	0
		mild dysuria	−3
		severe dysuria	−6
total score			29

* The Hirabayashi method is used to determine a patient's recovery rate: recovery rate = (final score − preoperative score) / (29 − preoperative score) × 100%. Abbreviation: ADLs = activities of daily living.

appropriate. The level of significance for all tests was defined as $p < 0.05$.

Results

Clinical Outcome

The mean JOA scores in the DLS and LCS groups were 11.2 and 12.5 before surgery and 21.6 and 22.5 at the final follow-up, respectively (Fig. 3 upper). The mean recovery rate was 58.7% in the DLS group and 62.0% in the LCS group; there was no significant difference in recovery rate between groups ($p = 0.49$). The JOA scores in the concave and convex groups were 10.7 and 11.5 before surgery and 21.8 and 21.8 at the final follow-up, respectively (Fig. 3 lower). The mean recovery rate was 58.6% in the convex and 60.6% in the concave group; there was no significant difference in recovery rates between the convex and concave groups ($p = 0.89$).

Radiographic Evaluation

The mean Cobb angles in the DLS group increased significantly from 12.7° preoperatively to 14.1° at final follow-up ($p = 0.0009$). The mean SWAs at L3–4 and L4–5 increased significantly from 6.2° and 4.1° preoperatively to 7.4° and 4.9° at final follow-up, respectively ($p = 0.05$ and 0.003, respectively). These data are summarized in Table 4.

The mean percentages of facet preservation in the LCS group were 73.4% on the approach side and 95.0% on the contralateral side at L3–4; they were 85.1% on the approach side and 95.9% on the contralateral side at

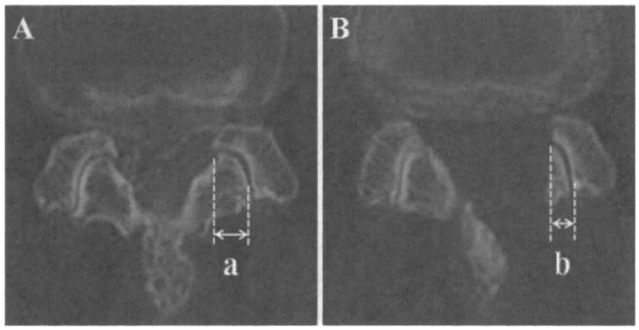

FIG. 2. Measurement of facet joint preservation on preoperative **(A)** and at final follow-up **(B)** CT scans. The length of the facet joint was measured using Scion Image software, and the percentage of facet preservation was calculated using the following equation: (percentage of facet preservation) = b/a × 100.

L4–5. The mean percentages of facet preservation in the DLS group were 79.4% on the approach side and 97.3% on the contralateral side at L3–4; they were 80.8% on the approach side and 96.1% on the contralateral side at L4–5. There was no significant difference between the DLS and LCS groups (Fig. 4 upper). The percentage of facet preservation was only compared between the convex and concave groups on the approach side. The mean percentages of facet preservation at L3–4 and L4–5 were 89.0% and 83.1% in the convex group and 67.3% and 77.6% in the concave group, respectively. The percentage of preserved facet was significantly higher in the convex group than the concave group at L3–4 ($p = 0.003$, Fig. 4 lower). The mean SWA in the concave group, but not in the convex group, was significantly increased at final

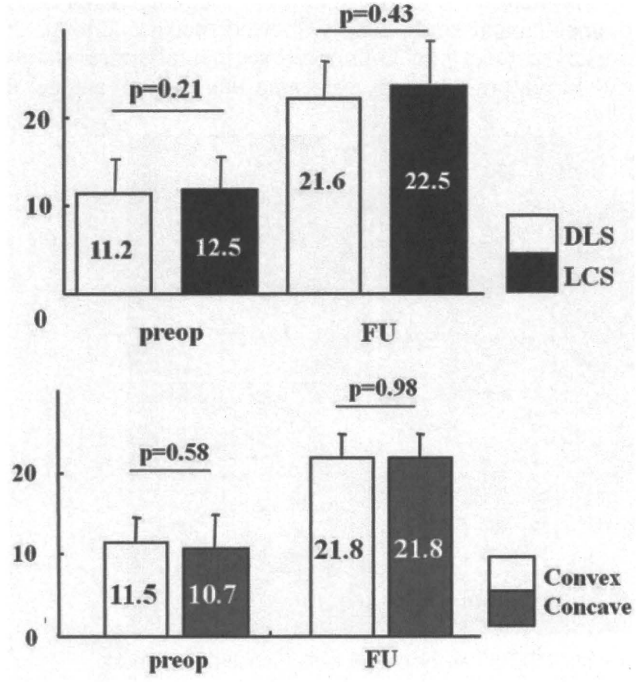

FIG. 3. **Upper:** Mean JOA Scale scores in the DLS and LCS groups; there was no significant difference between the groups. **Lower:** Mean JOA Scale scores in the convex and concave groups; there was no significant difference between groups. FU = final follow-up.

TABLE 4: Radiographic evaluation in DLS group*

Angle (°)	Preop	Follow-Up	p Value
Cobb angle	12.7 ± 3.2	14.1 ± 4.3	0.0009
SWA			
L3–4	6.2 ± 3.1	7.4 ± 3.9	0.05
L4–5	4.1 ± 2.6	4.9 ± 2.7	0.003

* Data presented as the mean ± SD and were analyzed using paired t-tests.

follow-up ($p = 0.01$ and 0.15, respectively; Table 5). The radiographic studies of both DLS subgroups are shown in Figs. 5 and 6. The facet joint on the approach side could be preserved using the convex approach, and the latest radiographs showed no obvious curve progression (Fig. 5). In contrast, poor facet preservation on the approach side with the concave approach led to curve progression and poor clinical outcome (Fig. 6).

Revision Surgery

Because of residual leg pain and low-back pain, 2 patients in the DLS group underwent additional fusion surgery during the follow-up period. Both patients underwent L3–4 and L4–5 MBDU via the concave approach. One patient complained of a recurrence of leg pain and severe low-back pain 6 months after initial surgery. A CT scan showed that the percentage of facet preservation on the concave side was 56%, and a radiograph showed that

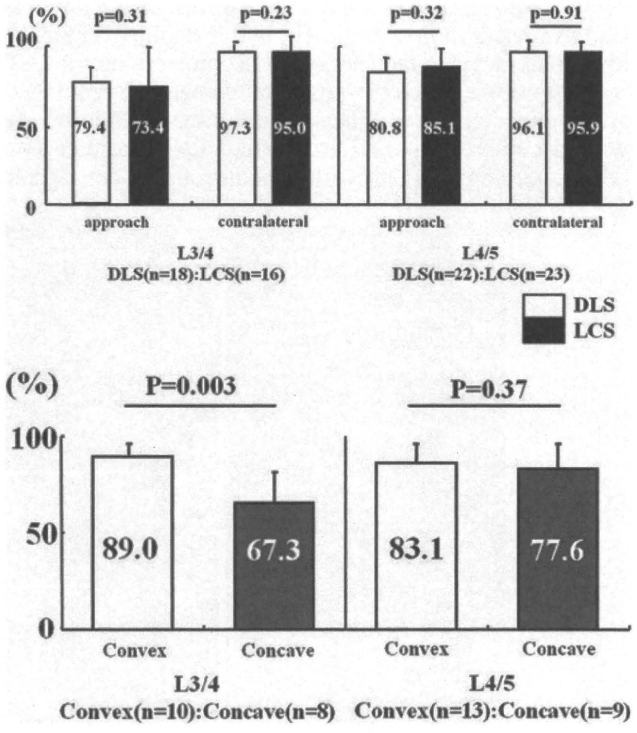

FIG. 4. **Upper:** Mean percentage of facet preservation in the DLS and LCS groups; there was no significant difference between groups. **Lower:** Mean percentage of facet preservation on the approach side in the degenerative lumbar scoliosis group. The percentage of preserved facet was significantly higher in the convex than in the concave group at L3–4 level ($p = 0.003$). n = number of treated segments.

TABLE 5: Differences in SWAs between convex and concave groups*

SWA (°)	Preop	Follow-Up	p Value
convex	5.41 ± 2.90	5.96 ± 3.52	0.15
concave	4.98 ± 3.19	6.10 ± 3.57	0.01

* Concave and convex indicate approach side of MBDU. Data are presented as the mean ± SD were analyzed using paired t-tests.

the SWA at L4–5 had progressed from 9° before surgery to 13° at revision surgery. The other patient complained of recurrent leg pain 1 year after initial surgery. Radiography and MR imaging showed L5–S1 foraminal stenosis. A huge osteophyte originating from the L5–S1 endplate compressed the L-5 nerve root anteriorly, and L5–S1 transforaminal lumbar interbody fusion was therefore performed.

Discussion

Degenerative lumbar scoliosis can be divided into 2 main types: degenerative scoliosis in conjunction with idiopathic scoliosis, and degenerative scoliosis with no previous scoliosis (de novo scoliosis).[2,18] Surgeons choose the surgical procedure based on the magnitude of the patient's spinal deformity, symptoms, and general condition. Decompressive surgery without fusion can sometimes result in good outcomes in patients with mild DLS, but some surgeons are concerned that in patients with DLS decompression can result in postsurgical spinal instability. The most important factor in the success of decompression for LCS is the preservation of the posterior elements. Decompressive laminectomy and bilateral unroofing can allow for a wide decompression, and acceptable clinical results have been reported in patients with radiculopathy or neurogenic claudication.[7,21] However, destruction or impairment of the pars interarticularis or facet joints can lead to postoperative spinal instability.[3] Additionally, a laminectomy requires wide paravertebral muscle stripping from the lamina, which can potentially denervate the paravertebral muscles and cause subsequent atrophy—changes that have been correlated with postoperative failed–back surgery syndrome.[17] Indications for decompressive laminectomy are therefore limited in patients with LCS when spinal instability is absent. An MBDU is a minimally invasive technique used to treat LCS.[20,23] It achieves good decompression without injuring the supra- or interspinous ligament complexes or contralateral paraspinal muscles, and it minimizes postoperative spinal instability. The present study demonstrated, in a minimum follow-up period of 2 years, a mean recovery rate of 58.7% following MBDU for DLS, which was equivalent to the recovery rate for LCS. Some authors recently presented a new minimally invasive decompression technique for LCS without spinal instability and demonstrated a recovery rate of approximately 60% (range 61%–67%).[6,8,19] Our recovery rate was similar to this and is thus considered to be acceptable. The Cobb angle and SWA were significantly increased at final follow-up, but the curve and disc wedging only increased by 0.5° in 1 year, and the progression in postoperative instability was therefore also deemed acceptable.[11] Although this study has certain limitations, in that MBDU was not indicated in all patients with DLS, DLS with mild segmental instability and mild spinal deformity was thought to be a good indication for this procedure.

The etiology of DLS is thought to involve asymmetrical disc degeneration leading to disc wedging and facet joint incongruity.[12,13] The facet joints thus play an important role in spinal stability, especially in DLS. A biomechanical study clearly showed that the amount of preserved facet joint influenced segmental spinal stability.[1] In the present study we found that the percentage of

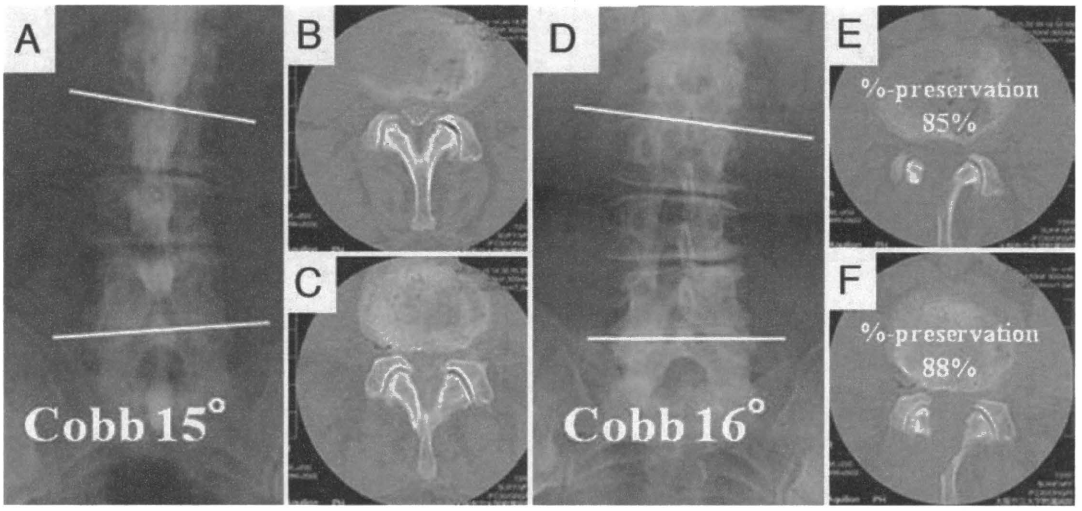

Fig. 5. Imaging studies obtained in a 74-year-old woman who underwent MBDU from the convex side. Preoperative standing AP radiograph **(A)** and preoperative axial CT scans of the L3–4 level **(B)** and L4–5 level **(C)**. The spinous processes are inclined to the contralateral side, providing a wider view from the convex than the concave side. Postoperative AP radiograph **(D)** after 5 years demonstrating no obvious postoperative spinal instability. Postoperative axial CT images at L3–4 **(E)** and L4–5 **(F)** revealing good preservation of the facet joints (percentage of facet preservation [%-preservation] on the approach side: L3–4, 85%; L4–5, 88%).

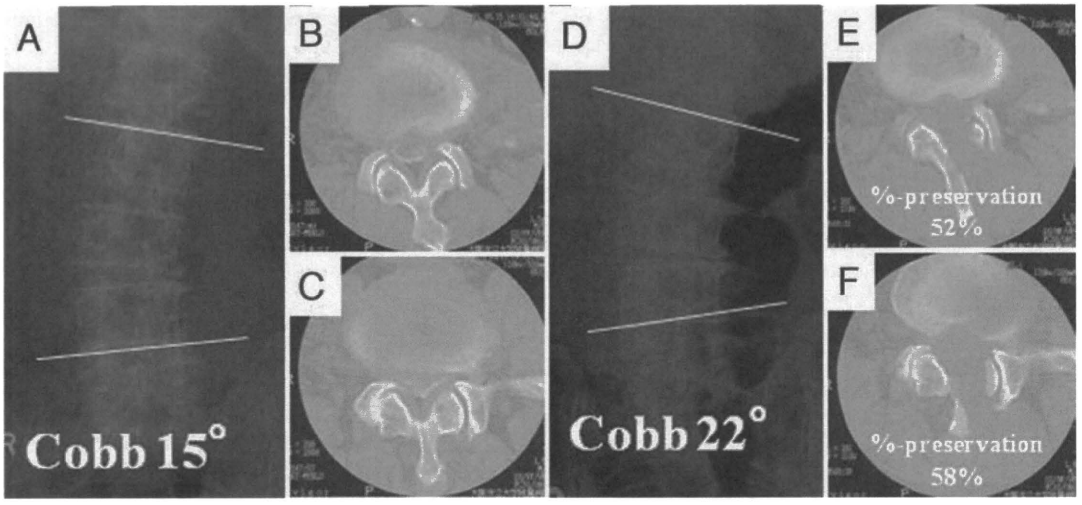

FIG. 6. Imaging studies acquired in a 71-year-old man who underwent MBDU on the concave side. Preoperative standing AP radiograph **(A)**, preoperative axial CT images at L3–4 **(B)** and L4–5 **(C)**. The spinous processes are inclined to the approach side, giving a narrower view from the concave side. Postoperative AP radiograph **(D)** acquired 2 years postoperatively demonstrating obvious postoperative spinal instability. Postoperative axial CT images at L3–4 **(E)** and L4–5 **(F)** showing poor preservation of the facet joints (percentage of facet preservation on the approach side: L3–4, 52%; L4–5, 58%).

facet preservation in the DLS group was approximately 80% on the approach side and 95% on the contralateral side, values that did not differ significantly from those in the LCS group. In DLS, spinal stenosis is often more severe on the concave than the convex side, and the concave side appears to be the symptomatic side.[9] We therefore tended to select the concave side as the approach side. However, the percentage preserved facet on the approach side was greater than that on the contralateral side. The poorer facet preservation on the approach side means that the approach-side effect must be taken into consideration when performing MBDU for DLS. Comparison of the preservation between the concave and convex approaches clearly showed that latter achieved significantly better facet preservation than the concave approach, because the spinous process tended to incline to the concave side due to of the vertebral rotation. The spinous process inclined to the contralateral side, providing a wider view from the convex in DLS. A wider view enables the surgeon to preserve the facet joint during surgery. Although there was no significant difference in recovery rates between the 2 groups, the SWA significantly increased only in the concave group. Additionally, the vertebra inclines to the concave side and then translates laterally. Thus, the facet joint on the concave side is more important than that on the convex side for stabilizing segmental instability. These results suggest that the convex approach should be preferred over the concave approach when performing MBDU in patients with DLS.

Conclusions

Unilateral-approach MBD can achieve good clinical outcomes in patients with DLS during a follow-up period exceeding 2 years. Additionally, it can reduce postoperative segmental spinal instability. A convex approach for MBD in patients with DLS allows good visualization, thus enabling surgeons to preserve the facet joints.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Matsumura, Namikawa. Acquisition of data: Matsumura, Namikawa, Terai, Tsujio, Suzuki. Analysis and interpretation of data: Matsumura, Namikawa, Dozono, Yasuda. Drafting the article: Matsumura, Nakamura. Critically revising the article: Matsumura. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Matsumura. Administrative/technical/material support: Matsumura. Study supervision: Matsumura, Nakamura.

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Journal of Cellular Physiology

Articular Cartilage Repair With Autologous Bone Marrow Mesenchymal Cells

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Articular cartilage defects that do not repair spontaneously induce osteoarthritic changes in joints over a long period of observation. In this study, we examined the usefulness of transplanting culture-expanded bone marrow mesenchymal cells into osteochondral defects of joints with cartilage defects. First, we performed experiments on rabbits and up on obtaining good results proceeded to perform the experiments on humans. Macroscopic and histological repair with this method was good, and good clinical results were obtained although there was no significant difference with the control group. Recent reports have indicated that this procedure is comparable to autologous chondrocyte implantation, and concluded that it was a good procedure because it required one step less than that required by surgery, reduced costs for patients, and minimized donor site morbidity. Although some reports have previously shown that progenitor cells formed a tumor when implanted into immune-deficient mice after long term in vitro culture, the safety of the cell transplantation was confirmed by our clinical experience. Thus, this procedure is useful, effective, and safe, but the repaired tissues were not always hyaline cartilage. To obtain better repair with this procedure, treatment approaches using some growth factors during in vitro culture or gene transfection are being explored. J. Cell. Physiol.

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Articular cartilage covers the ends of bones that form diarthrodial joints, and works as a lubricant and a shock absorber. Photomicroscopy reveals that histologically, articular cartilage is hyaline cartilage tissue because the intercellular matrix shows collapsed structure, and the tissue has no blood, lymphatic, or nerve supply.

Historically, articular cartilage has been considered to have only a weak capacity for repair, as reported by Hunter (1743) 250 years ago. It has been generally accepted that injuries that do not penetrate the subchondral bone (partial-thickness defects) are not repaired, while those that penetrate the subchondral bone (full-thickness defects) are repaired with the formation of various types of tissues, from a fibrous tissue to fibrocartilage. However, the reparative tissue, even that which is histologically like hyaline cartilage, lacks the biochemical capabilities to express some cartilage-specific molecules, and its biomechanical durability is substantially inferior to that of age-matched normal articular cartilage (Hunziker, 2002). The cartilage repair responses are different for individuals of different ages and for different species of animals, and such responses depend upon the physiological status of the animal, as well as the nature and extent of the injury.

What happens when such articular cartilage are left untreated? Until recently, many clinicians have been thinking that articular cartilage defects were not a major problem because they caused few clinical problems, at least during short observation periods. However, recently, some reports revealed that clinical symptoms or radiological changes due to articular cartilage defects become prominent when observed for more than 10 years (Messner and Gillquist, 1996; Shelbourne et al., 2003). Thus, it is now generally thought that articular cartilage should be repaired to prevent subsequent osteoarthritic changes. Articular cartilage defects are a major clinical problem; however, presently there is no treatment that is widely accepted to regeneratively repair these lesions. Currently, there is no satisfactory clinical technique for repairing articular cartilage defects. Current clinical practice usually involves bone marrow stimulation technique, in which subchondral bone is broken to facilitate cartilage repair from bone marrow-derived cells and cytokines, and consists of multiple perforations (Pridie, 1959), abrasions (Johnson, 1986), and micro-fractures (Steadman et al., 2003). However, with this procedure, cartilage defects are most often repaired with fibrocartilage, which is known to be biochemically and biomechanically different from normal hyaline cartilage and this tissue subsequently undergoes degeneration (Hunziker, 2002). Recent studies explored the usefulness of autologous chondrocyte implantation (ACI) (Brittberg et al., 1994) and mosaicplasty (Hangody et al., 2004; Matsusue et al., 1993) were explored. We can repair small articular cartilage defects using these techniques, although their effectiveness is still controversial. Even after ACI and mosaicplasty, some defects continued to persist in the articular cartilage, albeit not in the main weight-bearing portions of the joint. In ACI, no evidence of effectiveness has been reported so far (Nakamura et al., 2009), and we have to perform another operation to obtain autologous cells.

It has been reported that cells isolated from postnatal mammalian bone marrow have the potential for differentiation into specific cells of mesenchymal tissues, such as bone and cartilage, when implanted in vivo (Ashton et al., 1980; Goshima et al., 1991); thus, adherent cells in bone marrow blood contain progenitor cells for bone and/or cartilage. We assumed that these cells were suitable to repair osteochondral defects of joints because they could differentiate into both bone and cartilage. Thus, we performed autologous culture-expanded bone marrow mesenchymal cell (BMMC) transplantation in a rabbit model.

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Cartilage Repair With BMMC
Rabbit experiment (Wakitani et al., 1994)

We collected autologous osteochondral progenitor cells from bone marrow. They were culture-expanded and embedded into a collagen gel. These cellular grafts were then transplanted into large (3 mm × 6 mm, 3 mm in depth) full-thickness defects in the weight-bearing articular surfaces of 68 rabbits. These transplants were then observed for up to 6 months after surgery.

As early as 2 weeks after the transplantation, the defect was mostly replaced with cartilage. The replacement of this repaired cartilage began in the deeper portion of the defect with vascularized bone. By 4 weeks after transplantation, the deeper portion of the defect had been almost completely replaced by bone, and 24 weeks after transplantation, subchondral bone was completely repaired without loss or alteration of the overlying articular cartilage. We assume that BMMC preparations rapidly and quantitatively differentiate into chondrocytes in the rabbit distal medial femoral condyle defect, as has been observed in subcutaneous implantation samples. We hypothesize that these donor chondrocytes and the cartilage tissue that they form is replaced by host-derived vascular and bone-forming cells up to the bone articular cartilage junction.

Repair of articular cartilage defect in humans

Because the usefulness of BMMC transplantation in repair of osteochondral joint defects has been confirmed in a rabbit model, we thought that this technique could be applied in humans. BMMC have a number of suitable properties. First, it is easy to obtain autologous cells. This can be achieved by the aspiration of blood from the bone marrow using local anesthesia, without major side effects. Another reason for our interest in using these cells is that because we can cause them to proliferate without their capacity for differentiation being lost, this technique can be applied to large articular cartilage defects.

Two patients presented in our clinic because their knee pain prevented them from walking normally (Wakitani et al., 2004b). After thorough examination, we concluded that the knee pain was due to the injured articular cartilage, because there was no other abnormality in their knees. There were no improvements in clinical symptoms despite conservative treatment for a few months, and we decided to repair the defect with BMMC transplantation. Three weeks before transplantation, bone marrow was aspirated from the iliac crest of each patient. After erythrocytes had been removed using dextran, the remaining nucleated cells were placed in culture. When the attached cells had reached subconfluence, they were subcultured to expand in culture. Adherent cells were subsequently collected, embedded in a collagen gel, and then transplanted into the articular cartilage defect in the patellae and covered with autologous periosteum. Six months after transplantation, clinical symptoms (pain and walking ability) improved considerably, and the improvement persisted for 9 years post-transplantation in one case and 7 years in the other; both patients have been satisfied with the outcome. As early as 2 months after transplantation, the defects were covered with tissue that showed slight metachromatic staining. Two years after the first and 1 year after the second transplantation, arthroscopy was performed and the defects were found to have been repaired with fibrocartilage. We confirmed that autologous BMMC transplantation was an effective approach for promoting the repair of articular cartilage defects. Now, 12 years in the first and 10 years in the second case have passed, and there has been no clinical problem.

In order to apply this technique to the repair of articular cartilage defects in human osteoarthritic knees, we transplanted autologous culture-expanded BMMC into the cartilage defect of osteoarthritic knee joints when the patients were undergoing high tibial osteotomy (HTO), and observed the repair tissue when they were undergoing surgery for removal of the Steinmann pins and staples that fixed the separated proximal tibia (Wakitani et al., 2002). Twenty-four patients with knee osteoarthritis (OA) who underwent HTO were included in this study. Fifteen were female and nine were male. The patients' average age was 63 years (range 49–70 years). Twelve received autologous bone marrow cell transplants, and 12 were cell-free controls. All subjects enrolled in this study gave their informed consent, as approved by the institutional committee on human research; this committee also found this protocol to be acceptable. BMMC were prepared in the same manner as in the former two cases. The mean transplanted cell number was 1.3×10^7. HTO was performed using dome osteotomy, fixed with two pins with a Charnley clamp and two staples. At the time of HTO for OA of the knee, we transplanted these cells embedded in collagen gels into the medial femoral condyle, where articular cartilage was lost and subchondral bone was eburnated. We abraded the eburnated subchondral bone, transplanted cells in collagen, and covered the bone with autologous periosteum collected from the antero-medial surface of tibia. The mean size of the abraded area was 14 mm × 35 mm. The mean follow-up period was 16 months. Although the clinical improvement was not significantly different, the arthroscopic and histological grading score was better in the cell-transplanted group than in the cell-free control group. As early as 6.3 weeks after transplantation, the defects were covered with white soft tissue, in which metachromasia was partially observed, and 42 weeks after transplantation, the defects were covered with white soft tissue that was much harder than that observed at 6.3 weeks but was still softer than the surrounding normal cartilage. In almost all areas of the repair tissue, metachromasia was observed, and the repair tissue appeared similar to hyaline cartilage. This repair was found to occur much earlier and to be better than that reported in HTO only or HTO with abrasion (Fujisawa et al., 1979; Akizuki et al., 1997). The untreated tibial articular cartilage defects were not repaired at all.

We analyzed the clinical results 64 months after transplantation (Wakitani et al., 2008). The clinical scores were not significantly different between the cell-transplanted and the control groups. Longer observation might be necessary to see the effect of cell transplantation. Another possibility is that BMMC transplantation is not so effective in the osteoarthritic knee because the environment of the OA knee may not be good for cells or because the age of the patients was high.

Other reports of cartilage repair with BMMC transplantation

Kuroda et al. (2007) reported that transplantation of BMMC into 20–30-mm, full-thickness articular cartilage repair defect in the weight-bearing area of the medial femoral condyle of a 31-year-old judo player was effective.

We reported BMMC transplantation into osteochondral defects in five knees (femur and patella) from three patients. A 31-year-old female (bilateral knees), a 46-year-old male, and a 42-year-old male (bilateral knees) underwent BMMC transplantation in their patellofemoral joints (Wakitani et al., 2007b). All patients had suffered from pain and clicking in their patellofemoral joints on motion. Because magnetic resonance imaging (MRI) revealed articular cartilage abnormalities in the patellofemoral joints, we performed arthroscopy to confirm the lesions. After arthroscopy, we decided to transplant autologous BMMC. In the case of the 31-year-old female patient, we found articular cartilage damage in both the femur and the patella. We removed the damaged articular cartilage, transplanted BMMC embedded in the collagen gel, and covered

the transplanted tissue with autologous periosteum. Improvements in clinical symptoms were observed in all patients.

Recently, we applied this technique to repair osteochondral defects in three elbows (humeral capitellum; Wakitani et al., 2006). BMMC transplantation in humeral capitellum was performed on three 14-year-old boys. All patients were throwing athletes and had been suffering from elbow pain during throwing motion. Range of motion was slightly restricted. As shown in X-ray film, separated bone fragment was observed in capitellum and diagnosed osteochondral dissecans. Because the separated fragment was large, unstable, and divided into small pieces, we decided to remove the fragment and to transplant autologous BMMC. Clinical symptoms were much improved in all patients.

Nejadnik et al. (2010) reported BMMC transplantation into 36 articular cartilage defects and followed up for 24 months. They compared the results with those of 36 ACI and concluded that BMMC transplantation showed comparable results with ACI. They reported that it was a good procedure because it required one step less of surgery, reduced costs for patients, and minimized donor site morbidity.

These were all reports of the BMMC transplantation for articular cartilage defects that we could find presently.

Discussion of BMMC transplantation

Autologous culture-expanded BMMC transplantation was shown to be effective in the repair of articular cartilage defects, although no evidence has been shown. Important advantages of the techniques described herein are obvious from the data provided. Although these progenitor cells are not abundant, we have been able to mitotically expand them in culture. These approaches have considerable relevance to the treatment of human cartilage defects, and provide the starting point for the refinement of a repair technology capable, in principle, of regenerating large areas of articular cartilage.

The number of reports of BMMC transplantation in human is limited. The reports of BMMC transplantation that we could find are shown above. Besides these, we could find some reports in scientific meetings in the world. However, the total number of BMMC transplantations is much less than that of ACI. The reason for this is that ACI was explored first and made available very early. Even in ACI, evidence of the effectiveness is still controversial (Knutsen et al., 2004, 2007). There is only one report of randomized controlled trial in BMMC transplantation, which is mentioned above (Hui et al., 2010). This report showed that the clinical effectiveness of BMMC transplantation is comparable to results with ACI, although BMMC transplantation had superiority in some procedures. We have to explore more to show the evidence of effectiveness of BMMC transplantation.

The repair tissues were not completely composed of hyaline cartilage. Theoretically, hyaline cartilage is preferable. These cells could be driven in vitro into the chondrogenic lineage using cytokines (Sekiya et al., 2001; Yamamoto et al., 2004; Nawata et al., 2005) or gene transfection (Ikeda et al., 2004; Katayama et al., 2004), and the resultant autogenetic chondrocytes would be transplanted into cartilage defects.

It has been reported that cells isolated from human marrow aspirates could be induced to differentiate into other mesenchymal lineages, such as adipocytic, chondrocytic, or osteocytic lineages in vitro (Johnstone et al., 1998; Pittenger et al., 1999). Furthermore, they are reported to differentiate into cells other than mesenchymal tissues, ectodermal (neurocyte; Kopen et al., 1999) and endodermal tissues (hepatocyte; Petersen et al., 1999) (transdifferentiation). Recently, these cells are considered to be a useful cell source to repair some kinds of tissues, such as bone, cartilage, tendon, muscle, heart, small vessel, liver, nerve, and so on.

Other Progenitor Cells

Further investigations have been performed throughout the world for the repair of articular cartilage defects with hyaline cartilage, using certain other types of cells. Osteochondral progenitor cells or mesenchymal stem cells have been reported to exist in many kinds of tissues, such as the synovium, muscle, and fat. Autologous cells of these tissues are easily obtained. Within these cells, synovial cells are reported to have the best capacity for differentiating into cartilage, and are expected to be used clinically (Sakaguchi et al., 2005). Fat-derived mesenchymal cells are noteworthy (Mochizuki et al., 2006). These days, much of the population has excess fat, making it relatively easy to collect a large quantity of autologous cells.

Allogeneic cell transplantation has been explored in animal models. We have reported that cartilage-like tissue, generated ectopically by muscle-derived cells in a diffusion chamber using bone morphogenetic protein (BMP)-2, is effective in repairing articular cartilage defects in rats (Nawata et al., 2005). We have also reported that cartilage-like tissue, generated ectopically by amnion-derived cells using BMP-2 is effective in repairing articular cartilage defects in rats (Wei et al., 2009). These methods might be a new technique of tissue engineering for the repair of articular cartilage defects. Embryonic stem (ES) cells or inducible pluripotent stem (iPS) cells are one of the most promising cell sources for many kinds of tissue repair. These cells can be used to repair osteochondral defects, but it is difficult to induce these cells to differentiate exclusively into chondrocytes. We have reported that when we transplant ES cells into joint spaces they form a teratoma and subsequently destroy the joint (Wakitani et al., 2003). However, we also reported that when they are transplanted into osteochondral defects they form cartilage and promote the repair process (Wakitani et al., 2004a). The mechanism of this phenomenon is unclear; the use of ES cells is expected to increase in the future.

Problems With Cell Transplantation

Tumorigenesis

It has been reported that human adult stem cells from fat tissues can transform after long-term culture (Rubio et al., 2005). To our knowledge, this is the first report of transformation of cultured mesenchymal cells from adult humans. Some reports that supported tumorigenesis (Røsland et al., 2009). In these reports, cells were cultured for extraordinarily long periods, several months. Cells reached senescence or crisis phase, and cells appeared afterwards that had karyotype abnormality and formed tumor when injected into mice. Extremely long culture in vitro may injure the karyotypes and promote tumorigenesis. However, there are some reports that denied tumorigenesis. (Bernardo et al., 2007; Meza-Zepeda et al., 2008). Transformation of cultured cells is a major problem in cell therapy. We have never observed tumor formation in any of our extensive number of animal experiments or in clinical cases of BMMC transplantation. Human somatic cells have limited capacity for cell division. The possibility cannot be excluded, but the transformation of cultured adult human BMMC is considered to be rare.

To confirm the safety of BMMC transplantation, we investigated the patients with BMMC transplantation. Between January 1998 and November 2008, 41 patients received 45 transplantations. Neither tumors nor infections were observed in between 5 and 137 months (mean 75 months) of follow-up. From this result, we concluded that autologous BMMC transplantation is a safe procedure (Wakitani et al., in press).

Assessment of articular cartilage repair

As we explained in this article, the effectiveness of ACI has not yet been shown. One of the reasons for this is that it is difficult to estimate the effectiveness of articular cartilage repair. Clinical symptoms of articular cartilage are not resolved. Some patients feel nothing, while others suffer from pain. Although clinical symptoms are very important, they are not objective.

We have to objectively estimate the effectiveness of articular cartilage repair. One of the means for performing objective assessments of repair is MRI. Using MRI, we can estimate the extent of repair of the defect with different materials, but it is difficult to estimate the quality of the repair tissue. In the near future, we will be able to estimate its quality by MRI, because studies to develop such techniques are ongoing.

Arthroscopic biopsy is currently the most reliable procedure for estimating the repair tissue quality. However, this is an invasive procedure. Arthroscopy itself is invasive, and the biopsy is even more so. Therefore, even if we consider arthroscopy to be acceptable, it is not acceptable to perform biopsy. Thus, arthroscopic assessment methods using ultrasound, etc. are now being explored (Hattori et al., 2005).

Biological markers for OA have been explored. Many researchers have tried to detect the metabolic products of articular cartilage components (proteoglycans, type II collagen, and non-collagenous proteins) in joint fluid or blood and thereby develop a marker of OA. Keratan sulfate (KS), chondroitin 6 sulfate (C6S), cartilage proteoglycan aggrecan turnover epitope (CS846), hyaluronan (HA), and cartilage oligomeric protein (COMP) were candidate markers, and have been reported to be markers of OA to some extent. We measured KS levels using high-performance liquid chromatography, which has been reported to be more accurate than enzyme-linked immunosorbent assay (ELISA), and showed that the serum concentration of KS was high in patients with early-stage damage of the articular cartilage undetectable by X-ray imaging. Serum KS may be suitable as a screening test for articular cartilage damage and to monitor the natural course of articular damage or repair (Wakitani et al., 2007a). We have reported that newly explored highly sensitive ELISA kit is effective in detecting the serum KS, for screening early OA in humans (Wakitani et al., 2010).

Xenogenic proteins

We usually add fetal calf serum (FCS) into the medium for cell culture. For BMMC culture, prior to 2001, we added FCS. Cows with bovine spongiform encephalopathy (BSE) have been found in the USA, so some investigators are now using FCS from Australia as BSE is not found in that country. However, it is possible that in future, cows in Australia will carry BSE. If possible, we should not use FCS when we culture human cells for transplantation. Following confirmation that BMMC could be multiplied with autologous serum, we used autologous serum, not FCS, in human cell culture for transplantation.

Subsequently, an additional problem has been pointed out. It has been reported that a nonhuman molecule (silica acid Neu5Gc) is expressed on human ES cells when they are cultured on mouse feeder layers, and that antibodies specific for this molecule kill the cells (Martin et al., 2005). This report indicated that it was possible that cultured human cells expressed molecules from animals when they were in contact with animal-derived materials. Both FCS and collagens sometimes used as delivery vehicles may also be associated with induction of the same phenomenon.

Conclusion

We transplanted autologous culture-expanded bone marrow mesenchymal cells into articular cartilage defects. Clinical symptoms were improved but the repair cartilage was not hyaline cartilage. To regenerate articular cartilage by cell transplantation, it is essential that cells proliferate without losing their capacity for differentiation. To find appropriate conditions, different culture conditions, mechanical stresses, growth factors, and gene transfection have all been explored, but these have not yet been applied clinically.

The safety of cells is important. It has been reported that long-term culture may induce karyotype abnormality and tumorigenesis; we think these are due to the extraordinarily long culture periods. Usual culture periods are not dangerous for cell transplantation, as we showed in clinical experience.

Thus, this procedure is one of the most useful, effective and safe, but the repaired tissues were not always hyaline cartilage. To obtain better repair with this procedure, treatments with some growth factors during in vitro culture or gene transfection are being explored.

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Clinical Outcome of Microsurgical Bilateral Decompression *via* Unilateral Approach for Lumbar Canal Stenosis

Minimum Five-Year Follow-up

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Study Design. A retrospective study.

Objective. To evaluate minimum 5-year clinical outcome and radiologic changes in patients who underwent microsurgical bilateral decompression *via* a unilateral approach.

Summary of Background Data. Some authors have reported satisfactory short-term results of minimally invasive decompressive procedures such as microscopic or microendoscopic decompressive laminotomy for lumbar spinal stenosis (LSS). However, there have been a few reports on the long-term clinical outcome of these procedures.

Methods. The study consisted of 57 patients who underwent this surgery and had been followed for at least 5 years. The preoperative diagnoses were LSS without instability in 27 patients, degenerative lumbar spondylolisthesis (DS) in 20 patients, and degenerative lumbar scoliosis (DLS) in 10 patients. The mean duration of follow-up was 6 years. Clinical outcome was evaluated by Japanese Orthopedic Association (JOA) score. Complications, rate of reoperation, and radiographic changes after surgery on plain radiograph were evaluated.

Results. The mean JOA score was 13.8 ± 3.6 points before surgery, and improved to 24.9 ± 3.1 points at 3 months and 22.6 ± 4.7 points at the latest follow-up. There were no significant differences in JOA score at the latest follow-up among patients with LSS, DS, and degenerative scoliosis (22.3 ± 5.3, 23.3 ± 4.4, and 21.6 ± 2.6, respectively). Four patients (7%) underwent reoperation; 2 had DS and 2 had DLS. The preoperative percentages of slippage in patients with LSS, DS, and DLS were 0.4% ± 2.2%, 13.2% ± 5.9%, and 0.0% ± 1.3%, respectively, whereas degrees of progression of slippage at latest follow-up were 1.2% ± 3.1%, 2.4% ± 4.7%, and 0.0% ± 0.0%, respectively. There were no significant differences in progression of slippage among these 3 disease groups.

Conclusion. Microsurgical bilateral decompression *via* a unilateral approach is a minimally invasive technique that yielded satisfactory surgical outcomes even on minimum 5-year follow-up.

Key words: minimally invasive surgery, long-term, lumbar spinal stenosis, degenerative lumbar spondylolisthesis, unilateral approach. **Spine 2010;XX:000–000**

Decompressive laminectomy has been widely used as a treatment for lumbar spinal stenosis. Although satisfactory surgical outcomes have been reported with it, instability following the procedure has become the greatest concern among surgeons as a cause of deterioration of symptoms.[1,2] Whether this procedure is indicated for patients with degenerative lumbar spondylolisthesis (DS) and degenerative lumbar scoliosis (DLS) is another important concern.

Less invasive surgery using microsurgical and endoscopic procedures has come to be more commonly used for the treatment of lumbar spinal stenosis (LSS) over the last decade. The point of these procedures is maximal preservation of structural components such as midline structures, facet joints, and paravertebral muscle to prevent postoperative instability. Microsurgical bilateral decompression *via* a unilateral approach was first described by Poletti.[3] The procedure was modified by McCulloch and Young and described in detail in 1998.[4] In this technique, the dural sac and bilateral nerve roots can be decompressed with preservation of the supra- or interspinous ligament complex as well as the contralateral paraspinal muscles and facet joints. Enlargement of the central parts of the spinal canal is achieved by dome-shaped undercutting of the laminae and resection of the ligamentum flavum on the contralateral side.[3–7] The technique of limited osteoplastic laminectomy by spinous process osteotomy preserves the midline osseoligamentous structures and limits the instability created by standard lumbar decompressive laminectomy.[8] In our institution, microsurgical bilateral decompression *via* a unilateral approach, a modified version of McCulloch's method, has been performed since 1998 for the treatment of degenerative lumbar disorders such as LSS, DS with less than 10° of angular instability, and DLS with less than a 25° Cobb angle. The purpose of this study was to investigate the clinical outcomes of this surgical procedure over longer than 5-year follow-up.

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Table 1. Patients Demographics

Average age	69.6 yrs (range, 46–86)
Gender	Men:women = 27:30
Average follow-up	6.0 yrs (range, 5–8 yrs)
Diagnosis	
Lumbar spinal stenosis (LSS)	27
Degenerative lumbar spondylolisthesis (DS)	20
Degenerative lumbar scoliosis (DLS)	10
No. levels decompressed	
1 level	33
2 level	23
3 level	1

■ Materials and Methods

Patients

Fifty-seven patients operated on by 1 senior author (H.M.) and with longer than 5-year follow-up were included in this study. The clinical indications for this surgical procedure were leg pain and/or leg numbness inducing intermittent claudication rather than back pain. Radiologic evaluation included radiograph examination, magnetic resonance imaging, myelography, dynamic radiograph examination, and CT-myelography. The radiologic indications for use of this surgical procedure were LSS without instability, DS with less than 10° of angular instability, and DLS with less than a 25° Cobb angle. There were 27 men and 30 women. The age at surgery ranged from 48 to 86 years, with a mean of 69.6 years, and the duration of follow-up ranged from 5 to 8 years, with a mean of 6 years. The preoperative diagnoses were LSS in 27 patients, DS in 20 patients, and DLS in 10 patients. When the radiologic degenerative changes were more extensive than expected based on the clinical findings, we routinely used selective nerve root block to decide the level of decompression. Thirty-three patients underwent single-level, 23 patients underwent 2-level, and 1 patient underwent 3-level decompression (Table 1). The level of surgery was L2–L3 in 3 patients, L3–L4 in 24 patients, L4–L5 in 49 patients, and L5–S1 in 4 patients.

Surgical Procedure

Microscopic bilateral decompression *via* a unilateral approach was modified from the method reported previously to complete decompression on the contralateral side.[3–7] The laminotomy was performed on the side of approach in the area of the ligamentum flavum insertion, and resection of the articular process was performed in trumpeted manner until the inner aspect of the pedicle, with slight tilting of the microscope laterally. After the side of approach had been completely decompressed, the operating table and the microscope were tilted about 15° to observe the contralateral side. The basal part of the spinous process of the caudal half of the cranial lamina and a small cranial portion of the caudal lamina were removed with a high-speed drill. Then the contralateral lamina was undercut with a high-speed air drill leaving the ligamentum flavum in place as protection for the dural sac and the nerve root. Following sufficient resection of the bony segment, the ligamentum flavum was removed *en bloc* with a curette, while protecting the dural sac and contralateral nerve root with a patty. With recognition of the inner aspect of the pedicle on the contralateral side, we confirmed adequate decompression of the contralateral side (Figure 1).

Clinical Evaluation

Two authors (H.T. and S.D.) not involved in the care of these patients reviewed all records. Operative time, blood loss, Japanese Orthopedic Association score (JOA score), complications, rate of reoperation, and deterioration of symptoms in the follow-up period were investigated. Clinical outcomes were evaluated based on JOA score before surgery, 3 months after surgery, 1 year after surgery, and at latest follow-up (Table 2). Rate of improvement was calculated as follows, as suggested by Hirabayashi *et al.*[9] The overall result was classified as excellent in the case of greater than 75% improvement ratio in score, and good for 50% to 75%, fair for 25% to 49%, and poor for 0% to 24% improvement. Anteroposterior (AP) and lateral preoperative plain radiographs, postoperative radiographs, and radiographs at latest follow-up were examined. On lateral radiographs, slippage ratio was measured by the Boxall method.[10] On the AP view, the angle of scoliosis was measured by the Cobb method and the lateral slippage ratio was measured by the Boxall method.[11]

Statistical Analysis

Values are the mean ± standard deviation. The degree of significance was determined by *post hoc* testing using the Bonfer-

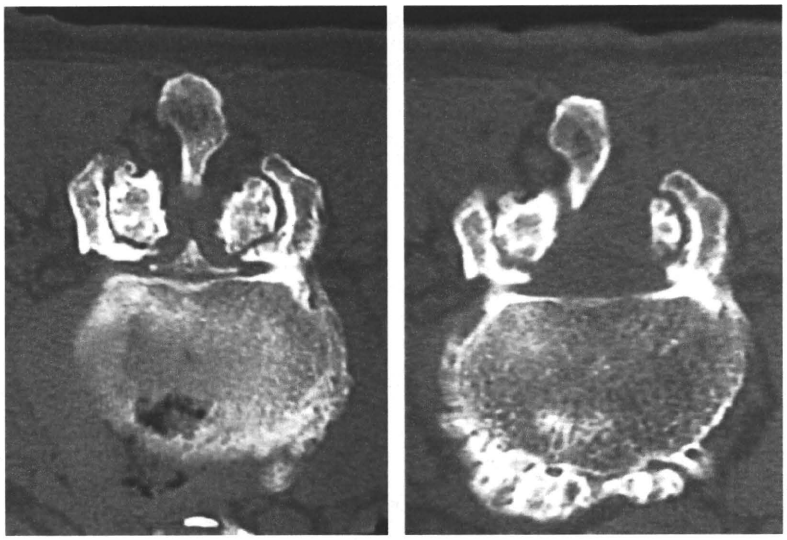

Figure 1. CT myelogram before operation and CT after operation. The lumbar spinal canal was adequately decompressed on the side of approach as well as the contralateral side.

Table 2. Criteria of the Japanese Orthopedic Association Lumbar Scores (JOA Score)

Item	Score
Subjective symptoms (9 points)	
Low-back pain	
None	3
Occasionally mile	2
Always present or sometimes	1
Always sever	0
Lower-limb pain and/or tingling	
None	3
Occasionally mile	2
Always present or sometimes	1
Always sever	0
Gait	
Normal	3
Able to walk at least 500 m, pain/numbness/ weakness present	2
Unable to walk at least 500 m, pain/numbness/ weakness present	1
Unable to walk at least 100 m, pain/numbness/ weakness present	0
Clinical signs (6 points)	
Strait leg raising (SLR)	
Normal	2
30°–70°	1
Less than 30°	0
Sensory disturbance	
Normal	2
Mild sensory disturbance	1
Apparent sensory disturbance	0
Motor disturbance	
Normal (MMT: normal)	2
Slightly weakness (MMT: good)	1
Markedly weakness (MMT: less than fair)	0
Restriction of activities of daily living (14 points)	
Turning over while lying	
None/moderate/severe	2/1/0
Standing	
None/moderate/severe	2/1/0
Washing face	
None/moderate/severe	2/1/0
Leaning forward	
None/moderate/severe	2/1/0
Sitting	
None/moderate/severe	2/1/0
Lifting or holding heavy object	
None/moderate/severe	2/1/0
Walking	
None/moderate/severe	2/1/0
Urinary bladder function (−6 points)	
Normal	0
Mild dysuria	−3
Severe dysuria	−6

MMT indicates manual muscle test.

roni method for continuous data and the χ^2 test for categorical data. An associated probability (P value) of <0.05 was considered significant.

■ Results

Clinical Results

The mean blood loss per level was 113.4 ± 74.8 mL, and the mean operative time per level was 134.2 ± 28.7 minutes.

The mean JOA score was 13.8 ± 3.6 points before surgery, but improved to 24.9 ± 3.1 points at 3 months, 25.6 ± 2.5 points at 1 year, and 22.6 ± 4.7 points at latest follow-up. The mean rate of improvement was 71.5% at 3 months, 73.5% at 1 year, and 57.9% at latest follow-up. On evaluation at latest follow-up, 11 patients were categorized as excellent (19.3%), 26 patients as good (45.6%), 17 patients as fair (29.8%), and 3 patients as poor (5.3%). In total, 64.9% of patients were rated as excellent or good. Nine patients exhibited gradual deterioration of symptoms during the follow-up period, and have undergone conservative treatment such as epidural block and root block. Of the 9 patients with symptom deterioration, 3 had LSS, 4 had DS, and 2 had DLS. Four patients (7%) underwent reoperation due to deterioration of symptoms. On evaluation by preoperative diagnosis, patients with LSS exhibited a 71.9% mean rate of improvement at 3 months and 54.1% at latest follow-up. For patients with DS, the corresponding percentages were 72.3% and 64.1%, whereas for patients with DLS, they were 75.1% and 51.6%. Deterioration of score was greatest for DLS, although there were no significant differences in JOA score at latest follow-up among LSS, DS, and DLS (Figure 2).

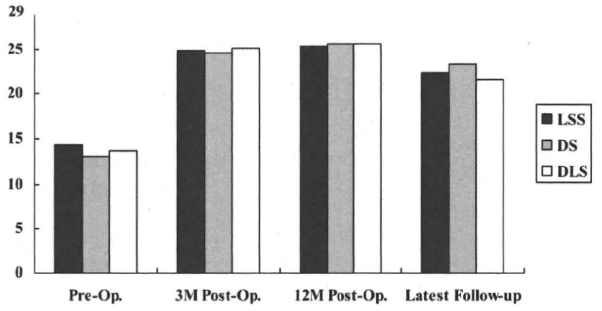

Figure 2. Average JOA scores before surgery, after surgery, and at the time of latest follow-up. Neither the ratio of improvement nor the score at latest follow-up differed among the preoperative diagnoses.

The 4 patients requiring reoperation included 2 with DS and 2 with DLS (Figure 3). No patient with LSS required reoperation. By type of reoperation, 1 patient with DS underwent repeat decompression and another with this condition underwent herniotomy. One patient with DLS underwent posterior lumbar interbody fusion at the level of operation during the study period, and another patient with DLS underwent second surgery at another

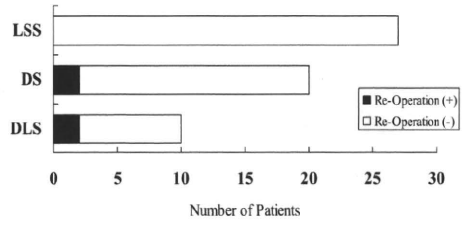

Figure 3. Numbers of patients requiring reoperation. The 4 patients requiring reoperation included 2 patients with degenerative lumbar spondylolisthesis (DS) and 2 patients with degenerative lumbar scoliosis (DLS). The rate of reoperation was 0% for lumbar spinal stenosis (LSS), 10% for degenerative lumbar spondylolisthesis, and 20% for degenerative lumbar scoliosis.

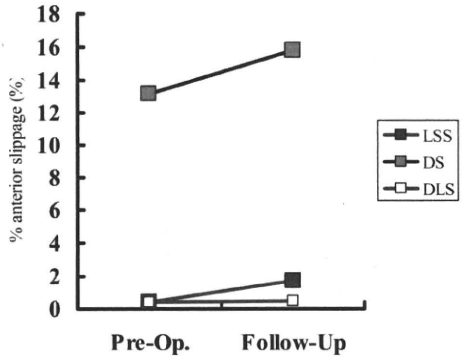

Figure 4. Progression of anterior slippage during the follow-up period. Progression of anterior slippage after this surgical procedure was 1.8% on average for longer than 5-year follow-up. The preoperative percentages of anterior slippage in patients with lumbar spinal stenosis (LSS), degenerative lumbar spondylolisthesis (DS), and degenerative lumbar scoliosis were 0.4% ± 2.2%, 13.2% ± 5.9%, and 0.0% ± 1.3%, and the percentages of slippage at latest follow-up were 1.8% ± 3.8%, 15.6% ± 7.9%, and 0.5% ± 1.4%, respectively.

level. Reoperation was performed a mean of 3.6 years (range, 1–7.3 years) after initial operation.

Radiologic Evaluation

The level of operation was L2–L3 in 3 patients, L3–L4 in 24 patients, L4–L5 in 49 patients, and L5–S1 in 4 patients. Progression of slippage was evaluated at the L4–L5 level. The preoperative percentages of anterior slippage ranged from 0 to 28.3, with a mean of 5.1% ± 7.3%. The percentages of anterior slippage at latest follow-up ranged from 0 to 37.5, with a mean of 6.9% ± 8.9%. Progression in anterior slippage after this surgical procedure was 1.8% during follow-up. The preoperative percentages of anterior slippage in patients with LSS, DS, and DLS were 0.4% ± 2.2%, 13.2% ± 5.9%, and 0.0% ± 1.3%, and the percentages of slippage at latest follow-up were 1.8% ± 3.8%, 15.6% ± 7.9%, and 0.5% ± 1.4%, respectively (Figure 4). The degrees of progression of slippage were 1.2% ± 3.1%, 2.4% ± 4.7%, and 0.0% ± 0.0%, respectively. There were no significant differences in progression of anterior slippage among these diseases. Number of cases of progression in slippage of more than 5% are shown in Figure 5. Progressive anterior slippage was found in 8 of 49 patients (16.3%), including 3 with LSS (3/23 13.0%) and 5 with DS (5/17 29.4%). No correlations were found between changes in clinical symptoms and progression of spondylolisthesis. The preoperative Cobb angle in DLS was 14.2° ± 7.4°, and progressed to 17.8° ± 9.6° at the latest follow-up. Preoperative lateral slippage in the coronal plane was found only in DLS; the preoperative value of 4.7% ± 6.2% increased slightly to 6.5% ± 6.8% after surgery, though this change was not significant. There were no patients with progression of lateral slippage of more than 5% after this procedure.

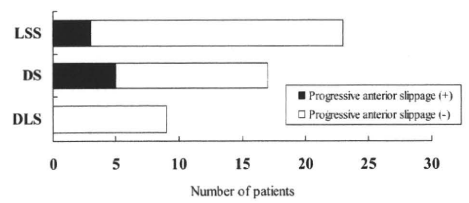

Figure 5. Numbers of patients with progression of slippage of more than 5%. Three such patients had lumbar spinal stenosis (LSS), with a frequency of new slippage of 13.0%, whereas 5 such patients had degenerative lumbar spondylolisthesis (DS), with a frequency of progression of slippage of 29.4%.

■ Discussion

LSS is a common lesion in elderly patients suffering from low back and leg pain with intermittent claudication. When conservative treatment fails, surgical treatment of this lesion becomes necessary, the most common of which is expansive laminectomy. Some authors have reported satisfactory results with decompressive laminectomy.[12–17] However, iatrogenic instability following laminectomy has become a problem.[1,2,18] Johnsson *et al* reported that postoperative slippage occurred in 18 of 45 patients (40%) who underwent laminectomies.[1] In their study, 65% of patients with DS exhibited a high risk of further slippage after operation and 20% of patients with LSS exhibited additional slippage. Mardjetko *et al* reviewed the incidence of progression of slippage after decompression and reported it to be 31%.[18] In some cases, spinal fusion combined with adequate decompression is therefore required.[19–21] A randomized trial and a study with alternating treatment assignments revealed better outcomes with decompression plus fusion than with conventional decompression alone.[20,22] However, some authors have suggested that patients treated with spinal fusion have a higher likelihood of greater blood loss, a longer operative time, and a higher rate of complications, and thus require more extensive revision surgery.[23–26] Thus, decompression surgery with clinical outcome equivalent to that of conventional decompression and less postoperative instability would be desirable.

McCulloch and Young developed unilateral laminotomy for bilateral ligamentectomy and reported a good or excellent outcome in 90.9% of 22 patients with acquired degenerative spinal stenosis.[4] Weiner *et al* reported limited osteoplastic laminectomy with spinous process osteotomy preserving the midline osseo-ligamentous structures, and found that 87% of patients reported high rates of satisfaction at 9 months' follow-up.[8] Thome *et al* reported that clinical outcome after unilateral laminectomy was equivalent to that with conventional laminectomy with a minimum follow-up period of 12 months.[27] As regard the long-term clinical outcome of less invasive decompression procedures, Oertel *et al* reported that 85.3% of 102 patients had excellent to fair results of surgery over 4 to 10 years (mean, 5.6 years) of follow-up, with a rate of reoperation of 11.8%.[28] Costa *et al* reported that 87.9% of 374 patients experienced clinical benefit and only 8% of patients suffered from segmental

instability at the treated level at a mean duration of follow-up of 30.3 months (range, 16–53 months).[29] Cavusoglu *et al* reported good results in 68% patients at 4 years, and noted that reoperation was not required for recurrent spinal stenosis at the same segments within 4 to 7 years.[30] In the present study, we evaluated clinical outcome and radiographic changes over a minimum 5-year follow-up, which ranged from 5 to 8 years with a mean of 6 years. The present study is thus the longest follow-up study of less invasive decompression procedures.

In our study, the rate of reoperation was 0% for LSS, 10% for DS, and 25% for DLS. The mean rate of reoperation was 7.0%. Katz *et al* reported that 23% of patients had undergone reoperation after 7- to 10-year follow-up for conventional decompressive surgery.[31] Iguchi *et al* reported that 3 of 37 patients (8.1%) who underwent decompression alone with longer than 10-year follow-up required additional surgery because of disc herniation at segments subjected to laminectomy.[15] Atlas *et al* found that 23% of patients who underwent decompression alone had required at least 1 additional lumbar spine operation by 10 years after their original procedure.[32] Compared with these previous reports on expansive laminectomy, the rate of reoperation was relatively low in our study. Whether this procedure should be performed for the treatment of DLS must be carefully determined.

In the present study, postoperative slippage occurred in 13% of cases of LSS and 29.4% of cases of DS. Matsunaga *et al* reported that progressive spondylolisthesis was observed in 34% of nonsurgically managed patients with DS during 10- to 18-year follow-up.[33] Yoshida *et al* reported that the rate of progression of slippage was 33.3% while that of new slippage was 12.0% over 11-year follow-up.[34] Mardjetko *et al* reviewed the incidence of progression of slippage after decompression and reported it to be 31%.[18] Compared with these reports, we found little progression of spinal slippage with the present procedure over a minimum 5-year follow-up. The radiographic changes after this procedure were similar to those described in other reports on the natural course of LSS and DS.

There are a few limitations to this study. First, this was a retrospective study without any control group. Second, the indications for this surgical procedure were limited to patients with less than 10° of angular instability in the case of DS and those with less than a 25° Cobb angle in the case of DLS. The usefulness of this procedure for patients with severe deformity or less stability is thus still unclear. However, the present study yielded the important finding that microsurgical bilateral decompression *via* a unilateral approach yielded satisfactory long-term outcome in patients with LSS and in some patients with DS or DLS.

■ Conclusion

Microsurgical bilateral decompression *via* a unilateral approach is a minimally invasive technique that yielded satisfactory surgical outcomes even with a minimum 5-year follow-up period. Good clinical outcome was obtained not only for LSS but also for DS and DLS. Spinal stability was superior to that with other expansive procedures even in cases of DS and DLS.

■ Key Points

- Microsurgical bilateral decompression *via* a unilateral approach is a minimally invasive technique that provided satisfactory clinical outcome for longer than 5-year follow-up.
- Good clinical outcome was obtained not only for LSS but also for DS and for DLS.
- Radiographic changes after this procedure were similar to those described in other reports on the natural course of LSS and DS.

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