

Evaluations of minimally invasive transforaminal lumbar interbody fusion performed with rhBMP-2

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Abstract

Background: The combination of minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) and recombinant human bone morphogenetic protein 2 (rhBMP-2) is widely used for its advantage of rapid recovery and improved bone fusion. However, no previous study has reported the synergistic effect of MIS-TLIF with rhBMP-2 in patients with degenerative lumbar disease (DLD). **Objective:** To investigate the radiographic and patient-reported outcomes (PROs) in patients with DLD who underwent MIS-TLIF with and without a low dose of rhBMP-2. **Methods:** We retrospectively reviewed 48 patients treated with MIS-TLIF from 2013 to 2016. The patients were classified into the rhBMP-2 group (n = 25) and non-rhBMP-2 group (n = 23). Fusion-related parameters were measured before and after the operation. Clinical data included the numeric rating scale (NRS) score, Japanese Orthopedic Association (JOA) scores, and the MOS 36-item short form health survey (SF-36) score, which were documented to evaluate the effect of surgery. **Results:** In the 48 patients who underwent MIS-TLIF, the operated disc was predominantly at the L4/5 and L5/S1 levels. ADH, MDH, and PDH increased significantly in both groups after surgery ($P < 0.05$). FH improved in the rhBMP-2 group, but not in the non-rhBMP-2 group. There was no obvious improvement in SA in both groups. Furthermore, the SL showed a significant difference in both groups and a significant improvement over the baseline. The LL showed significant improvement in the two groups at the early follow-up ($P < 0.05$), but the improvement did not persist. Cage subsidence had no significant effect on different subsidence grades. In addition, no differences in cage subsidence were observed in different types of modic change (MC), except for MC 0 in both groups. There was no difference in PROs even though all clinical outcomes improved significantly during the postoperative follow-up period in both groups. **Conclusion:** MIS-TLIF with the low doses of rhBMP-2 resulted in an improvement in radiographic and clinical results, but not a longer-lasting restoration for radiographic outcomes. Cage subsidence is not associated with the MC. Further, our clinical data demonstrated no difference between both groups.

Background

Since its inception, minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) has gained popularity because it offers advantages such as smaller iatrogenic injury, less blood loss, a lower possibility of surgical site infection, and alleviation of adjacent segment degeneration.[1] Additionally, the TLIF procedure shows advantages in the treatment of degenerative diseases because of its ability to preserve the bony structure and pars interarticularis and restore the intervertebral height, foraminal height (FH), and segmental lordosis.[2] However, cage migration within the disc space may cause progressive spinal deformity and narrowing disc space or even intraoperative injuries.[3]

BMP is a member of the $TGF\beta$ superfamily and promotes bone formation by regulating cell differentiation and matrix synthesis.[4] Administration of rhBMP-2, a subtype of BMP, has been combined with the MIS-TLIF procedure due to higher integration rates.[5] However, no previous studies have investigated the radiologic parameters and clinical outcomes of rhBMP-2 administration in the MIS-TLIF procedure. Prior literature demonstrated the presence of adverse effects, such as pseudarthrosis and ectopic bone formation, in many patients.[6] Other studies have further stratified the relationship between clinical outcomes and rhBMP-2 dosage.[7] Although promising results were obtained in rhBMP-2-assisted spinal fusion, the effect was poor since researchers failed to control the confounding variables because of the lack of a specific protocol to evaluate the outcome of surgery.[8] However, recent literature has documented that distinct radiographic changes can be assessed to evaluate the effect of rhBMP-2-assisted spinal fusion. Fusion-related sagittal parameters, cage subsidence, and MC can be well detected on CT or MRI. Jang et al. suggested that there is a relationship between sagittal parameters, cage subsidence, and clinical outcomes in degenerative cervical disease.[9] However, the radiographic sagittal parameters of MIS-TLIF performed with and without rhBMP-2 in the disk space have not been fully evaluated.

In the current study, we reviewed our experience with MIS-TLIF to elucidate the effect of rhBMP on the sagittal parameters, cage subsidence, and MC of the operated segment. We aim to explore potential relationships between use of rhBMP-2 and improvement in radiologic parameters and clinical outcomes. Further, possible correlations of these parameters were investigated.

Methods

This study identified 48 patients who had complaints of low back pain or neurologic symptoms. Data for age, gender, and operated level were collected from inpatient medical records. Single or two-level MIS-TLIF procedures were performed on all patients from March 2013 to February 2016. This protocol was approved by the ethics committee of the Affiliated People's Hospital with Jiangsu University. All patients gave written informed consent for their information to be stored in the hospital database and used for research. This study was conducted according to the principles expressed in the Declaration of Helsinki. Our exclusion criteria were as follows: spinal fracture, lumbar infection and tumor, prior history of lumbar surgery, and MIS-TLIF operated on levels above the lumbar spine. A total of 25 patients received additional rhBMP-2 treatment (rhBMP-2 group), while 27 patients did not receive rhBMP-2 treatment (non-rhBMP-2 group). We collected clinical data from inpatient medical records, pre- and postoperative plain radiographs, and postoperative CT or MR images. All patients were contacted by cellphone to collect missing information. Demographics and procedure data listed in Table 1 were recorded prospectively for both groups.

Radiologic outcome evaluation

We measured anterior disc height (ADH), middle disc height (MDH), posterior disc height (PDH), segmental angle (SA), segmental lordosis (SL), and foraminal height (FH) of the operated levels and lumbar lordosis (LL) on pre- and postoperative radiographs to quantify the postoperative distraction of disc height and indirect decompression. We evaluated disk height by measuring the ADH, MDH, and PDH. The ADH was defined as the distance between the anterosuperior edge and the anteroinferior edge, PDH was defined as the distance between the posterior inferior edge and the posterosuperior edge, whereas the MDH was defined as the distance from the inferior endplate to the superior endplate at the midpoints of the vertebral body. The SA was defined as the angle between the superior endplate and the inferior endplate of the operated level. The SL was the angle between the superior endplate and the inferior endplate of the segment. The LL was defined as the angle between the superior endplate of L1 and the superior endplate of S1. (Figure 1) Cage subsidence was evaluated by measuring migration of the cage into the endplate. Cage subsidence was defined as a mean of the sum of the left and right cage subsidence on CT (Figure 2).

Clinical outcome evaluation

Pain and functional results were documented during the preoperative period and 1, 3, 6, and 12 months postoperatively to evaluate the clinical outcomes. The clinical results included numeric rating scale (NRS) scores, Japanese Orthopedic Association (JOA) scores, and the MOS 36-item short form health survey (SF-36) scores. The NRS scores were adopted to evaluate the intensity of low back pain as well as leg pain. The JOA and SF-36 scores were used to evaluate the daily functionality of patients.

Statistical analyses

We performed data analysis with SPSS (version 21.0, SPSS Inc, Chicago, IL). We compared the pre- and postoperative radiologic and clinical outcomes with independent and paired Student t-tests. The mean values of the two groups were compared by one-way ANOVA. We calculated the correlation between the variables using Pearson correlation coefficients and Spearman correlation coefficients. *P* values less than 0.05 were considered statistically significant.

Results

The patients presented with spondylolisthesis, spinal stenosis, and recurrent disc herniation. Both groups showed no significant difference with respect to mean age and gender distribution. (Table 1)

Radiologic evaluation

The postoperative ADH, MDH, and PDH at early follow-up differed significantly from the preoperative and final follow-up values in both groups ($P < 0.05$) (Figure 3). The postoperative FH at early follow-up differed significantly from the preoperative and final follow-up values in the rhBMP-2 group ($P < 0.05$). Furthermore, the postoperative FH at the final follow-up differed significantly from the preoperative and early follow-up values in the non-rhBMP-2 group ($P < 0.05$). The segment angle at the final follow-up differed significantly from the early follow-up value in the rhBMP-2 group ($P < 0.05$). The SL in the rhBMP-2 group at the final follow-up period differed significantly from the baseline value and the SL evaluated at the final follow-up in the non-rhBMP-2 group ($P < 0.05$). The LL at early follow-up in the rhBMP-2 group differed significantly from the LL evaluated at early follow-up in the non-rhBMP-2 group ($P < 0.05$) (Table 2) (Figure 4).

Our results revealed a stronger correlation between ADH and MDH ($r = 0.660$; $P = 0.001$). The MDH was correlated with the PDH ($r = 0.656$; $P = 0.001$). The PDH was correlated with the FH ($r = 0.449$; $P = 0.024$). The FH was correlated with the NRS leg ($r = 0.476$; $P = 0.016$). The SA was correlated with the SL ($r = 0.427$; $P = 0.033$). The SL was also correlated with the LL ($r = 0.478$; $P = 0.016$), NRS back ($r = 0.427$; $P = 0.033$), and NRS leg ($r = 0.409$; $P = 0.043$). The LL was correlated with the NRS back ($r = 0.400$; $P = 0.048$). Cage subsidence or MC were not related to postoperative sagittal parameters (Data not shown). (Table 3)

Subsidence and modic change

Modic change was classified as type 0 in 10 rhBMP-2 cases and 11 non-rhBMP-2 cases, type I in one rhBMP-2 case and two non-rhBMP-2 cases, type II in 15 rhBMP-2 cases and 12 non-rhBMP-2 cases, and type III in one rhBMP-2 case and no non-rhBMP-2 cases. Grade 1 subsidence was 0.61 ± 0.23 mm in the rhBMP-2 group and 0.71 ± 0.12 mm in the non-rhBMP-2 group, grade 2 subsidence was 1.47 ± 0.31 mm in the rhBMP-2 group and 1.76 ± 0.46 mm in the non-rhBMP-2 group, and grade 3 subsidence was 3.01 ± 0.00 mm in the non-rhBMP-2 group (Table 4). Cage subsidence was positively related to the type of MC, with the most severe MC showing maximum cage subsidence. However, cage subsidence showed no difference in different types of MC, except for the normal endplate. (Figure 5)

Clinical evaluation

The NRS scores for back pain significantly improved 6 months postoperatively (from 6.32 ± 0.73 to 2.12 ± 0.81 in the rhBMP-2 group and from 6.26 ± 0.79 to 2.01 ± 0.29 in the non-rhBMP-2 group, $P < 0.05$). NRS scores for leg pain also significantly increased 6 months postoperatively (from 6.32 ± 0.73 to 2.04 ± 0.52 in the rhBMP-2 group and from 6.01 ± 0.59 to 1.78 ± 0.65 in the non-rhBMP-2 group, $P < 0.05$). The JOA score significantly improved at 1 month in both groups (from 15.28 ± 5.71 to 23.09 ± 2.99 for the rhBMP-2 group and from 14.57 ± 2.83 to 23.65 ± 0.71 for the non-rhBMP-2 group, $P < 0.05$). SF-36 scores significantly improved at the final follow-up (from 45.49 ± 3.13 to 70.22 ± 5.08 in the rhBMP-2 group and from 45.99 ± 5.56 to 70.33 ± 5.68 in the non-rhBMP-2 group, $P < 0.05$). (Figure 6)

Complications

No cases of intraoperative complications, such as neurological damage, postoperative alterations in sexual activity, or ejaculation-related pain were found. Different degrees of cage subsidence were found in all cases during the follow-up period. Overall, our results demonstrated a low complication rate for MIS-TLIF using rhBMP-2.

Discussion

Dose of rhBMP-2

rhBMP-2 has been proven to be effective in relieving donor site pain and reduce morbidity.[10] However, rhBMP-2 also shows a series of inflammatory dose-related complications, including radiculitis, osteolysis, and ectopic bone formation. [11] Owens K et al. demonstrated a modest complication rate in MIS-TLIF procedure, with rhBMP-2-associated complications occurring infrequently.[12] Even though the optimal rhBMP-2 dose in TLIF procedures remains a matter of

debate, Villavicencio AT et al. reported that there was no correlation between the dose of rhBMP-2 and the incidence of rhBMP-2-induced radiculitis.[13] Alan T et al. confirmed the effectiveness and safety of a combination of MIS-TLIF and rhBMP-2 in lumbar fusion whereas no significant difference was found in clinical outcome between MIS-TLIF and open procedures.[13] A few years later, they adopted a wide dose range (2–12 mg) of rhBMP-2. Their retrospective study did not determine the relationship between the rhBMP-2 doses and the radicular symptoms. [14] To date, the 4-6 mg/level dose of rhBMP-2 is widely adopted in clinical practice. [15] Here, our adoption of low rhBMP-2 dosage (2 mg/ level) was effective and safe in the MIS-TLIF procedures and yielded satisfactory radiological and clinical outcomes.

Fusion rate

Many studies assessing long-term follow-up data have shown that poor bone fusion results in degeneration of the vertebral body, functional disability, lumbar spine instability, and pain. [16, 17] We observed a higher fusion rate in the rhBMP-2 group than in the non-rhBMP-2 group, which was consistent with prior studies reporting a higher fusion rate compared with autologous bone grafts. [18] Vaidya et al. demonstrated that radiologic signs of fusion in patients receiving allografts and rhBMP-2 appeared earlier than those in patients not receiving rhBMP-2, with the signs appearing at 6 and 19 months, respectively. However, the exact time of fusion is difficult to determine because it is unrealistic for return visit patients to undergo surgical reexploration in the short time interval after surgery. We confirmed that application of low doses of rhBMP-2 leads to a significantly different fusion rate between both groups at 3 months postoperatively. Radiographic evidence of reexploration for recurrence of pain suggests that the cage was securely fused by 8-12 weeks, which indicates that the actual process began sooner than that detected on radiography. [19]

Sagittal parameters

Previous studies demonstrated that disc degeneration causes an increase in ADH and PDH. [20, 21] Hsieh et al. found that SL decreased at the operated segment. [22] The compensatory increase in PDH relative to the increase in ADH led to the maintenance of the SL. Biomechanical research has suggested that procedures improve the disc height and FH deficits caused by disc degeneration. [23] We found a significant increase in ADH, MDH, and PDH at the operated level in both groups. The disc height and FH in the rhBMP-2 group decreased more significantly than that in the non-rhBMP-2 group.

Further, recent studies involving MIS-TLIF evaluated SL and presented variable results. Some reported an insufficient ability of MIS-TLIF to restore SL at the surgical level, whereas others showed substantial increases in SL. We found a significant increase in LL in patients with DLD, which was consistent with a previous study that confirmed that the interbody fusion is highly effective in improving LL.[24] Some investigators demonstrated an association between postoperative LL and better clinical outcomes.

Previous studies evaluated short- and long-term complications associated with off-label rhBMP-2 use with TLIF. Some studies suggest that these complications may be dose-positive, and the higher the dose, the greater the probability of complications. [25] Complications and results were analyzed by BMP dose and primary versus revision surgery. Based on these results, surgical technique and rhBMP-2 dose recommendations were proposed.

Disc height restoration

No consensus regarding the results of the restoration of disc height was reached. Liu et al. suggested that the improvement in disc space height plays a vital role in facet joint subluxation. [26] Kaito et al. proposed that the distraction of disc space was a potent risk factor for the progression of adjacent segment disease (ASD), which may affect clinical outcomes of patients. [27] Michael C et al. found that disc height restoration was positively associated with segmental lordosis. [28] Our results are the first to investigate the effect of rhBMP-2 in the restoration of disc height. However, even though rhBMP-2 slightly slowed down restoration of disc height and FH to some extent, we did not find any significant differences in the two groups.

Biomechanical studies have proven that diminished LL may increase the risk of ASD. [29] Kepler et al. reported that the decrease in LL was related to worse clinical outcomes, which was consistent with our results. [30] Hence, our results showed that rhBMP-2 increased postoperative SL and LL by 0.9° and 3.1°, thus improving clinical outcomes by restoring sagittal alignment. Some researchers found a relationship between restoration of LL and improvement in clinical outcomes. [31] However, the relationship between radiographic improvement and clinical outcomes was not found in the current study. Postoperative maintenance of the SL may lead to a compensatory gain of adjacent segment lordosis, which is confirmed by the correlation between the postoperative LL and the SL of the adjacent levels.

Subsidence and MC

Several factors, including age, sex, and bone mineral density were reported to affect cage subsidence in MIS-TLIF. Tokuhashi et al. demonstrated that the average cage subsidence was 2.7 ± 3.4 mm on the caudal surface and 4.0 ± 2.3 mm on the cranial surface. [32] Their results were higher than those reported in the current study. The differences in cage subsidence may be attributable to the different measurement methods. CT could precisely measure the amount of subsidence during the bone remodeling process, so the average subsidence and prevalence of subsidence measured by plain radiographs were lower than those reported in other studies that used CT. David et al. reported that intact endplates increased strength and resistance to subsidence. [33] MC was associated with vertebral body structural changes such as disc herniation and vertebral endplate defect. [34] We found that cage subsidence in a different type of MC showed no significant difference except for normal endplate. Our result indicates that MC in the vertebral body may affect endplate preparation, which plays a vital role in preventing cage subsidence. However, our data did not show an improvement in cage subsidence in the rhBMP-2 group.

Clinical outcome

Even though all clinical outcomes improved significantly in the two groups, we found no significant difference between the groups. We demonstrated that the degrees of sagittal correction, fusion rates, and incidence of cage migration were not related with clinical outcomes in the first 12 months postoperatively. Compared with prior studies, our procedure integrated the advantages of MIS-TLIF and rhBMP-2 and confirmed that MIS-TLIF combined with rhBMP-2 is a better choice for lumbar degenerative disease.

Limitations

Some limitations could not be avoided in this retrospective study. First, as the properties of L4-5 and L5-S1 are different in terms of their contribution to disc height, FH, SA, and the dimensions of the disc space, the bias resulting from the different numbers of operated levels could not be avoided. Second, our sample size was too small to obtain an accurate evaluation of the results. Third, long-term postoperative clinical assessment data were unavailable because some patients were lost to follow-up, making it impossible to reliably assess the clinical outcome of surgery. Fourth, our results did not identify the optimal rhBMP-2 dose in DLD surgeries. Prospective, randomized clinical trials are needed to determine the optimal rhBMP-2 dosage and complications.

Conclusions

We conclude from this research that single-level MIS-TLIF combined with or without rhBMP-2 significantly increased the ADH, MDH, and PDH but not the SL. However, LL shows a slight but significant improvement resulting from an increase in the cranial SL. A higher fusion rate was observed in the rhBMP-2 group. However, intraoperative use of rhBMP-2 in the MIS-TLIF procedure has no effect on postoperative clinical outcomes since the NRS scores, JOA scores, and SF-36 scores in both groups were not statistically different.

Abbreviations

ADH: anterior disc height; MDH: middle disc height; PDH: posterior disc height ; FH: foraminal height; SA:segmental angle; SL: segmental lordosis; LL: lumbar lordosis; NRS: numeric rating scale score; JOA: Japanese Orthopedic Association scores;

SF-36: the MOS 36-item short form health survey score;

MIS-TLIF: minimally invasive transforaminal lumbar interbody fusion;

rhBMP-2: recombinant human bone morphogenetic protein 2;

DLD: degenerative lumbar disease;

ASD: adjacent segment disease;

MC: modic change

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Affiliated People's Hospital of Jiangsu University; due to the retrospective nature of the study, the need for informed consent was waived.

Consent for Publication

Not applicable.

Availability of data and material

All data has been showed in tables and picutres.

Competing interests:

The authors declare that they have no conflict of interest.

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Authors' contributions

BL, YTH, DL and LW conceived and designed the study; XY, JSY, and AQH performed the experiments; XY and AQH analysed the data; BL, YTH and RGC wrote the paper; AQH, JSY, and LW reviewed and edited the manuscript. BL performed major revision and minor revision. All authors read and approved the manuscript.

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Tables

Table 1. Patient baseline characteristics

Demographic Data	MIS-TLIF		P Value
	rhBMP=25	Non-rhBMP=27	
Age, years	58.2±9.2	57.8±8.7	0.779
Female, n (%)	17/25	15/23	0.357
Diagnosis			0.490
Spondylolisthesis	6	11	
Spinal stenosis	9	9	
Recurrent disc herniation	7	10	
Level			0.443
L3-4	2	2	
L4-5	21	19	
L5-S1	3	7	

Table 2. Clinical outcomes before and after surgery

		Group	Pre-op	Early follow up	Final follow up
ADH	23	non-rhBMP-2	12.13±2.74	15.91±2.48a	12.27±3.58b
	25	rhBMP-2	12.6±2.6	15.17±2.73a	12.18±2.61b
MDH	23	non-rhBMP-2	10.72±2.00	12.80±2.10a	10.72±2.05b
	25	rhBMP-2	10.59±2.08	12.68±1.84a	10.70±1.69b
PDH	23	non-rhBMP-2	8.23±1.44	8.73±1.58	7.74±1.48b
	25	rhBMP-2	7.62±1.51	9.36±1.54a	7.78±1.34b
FH	23	non-rhBMP-2	18.50±2.72	19.18±2.69	17.5±2.72ab
	25	rhBMP-2	18.14±2.86	20.55±2.10a	18.40±2.26b
SA	23	non-rhBMP-2	8.60±4.71	8.38±3.11	9.33±3.46
	25	rhBMP-2	9.09±3.52	8.33±3.07	10.12±3.76b
SL	23	non-rhBMP-2	17.03±6.30	18.99±4.29	19.51±4.90*
	25	rhBMP-2	17.01±6.89	15.72±7.22	15.26±7.36a
LL	23	non-rhBMP-2	39.58±14.61	40.86±10.08*	44.68±11.58
	25	rhBMP-2	38.56±15.13	34.80±10.51	40.7±12.88b

Note: ^aP < 0.05 vs. presurgery; ^bP < 0.05 vs early follow-up.

*indicates P < 0.05 between the non-rhBMP-2 and rhBMP-2 groups

Table 3. Correlation between postoperative radiologic parameters and clinical outcomes

	ADH	MDH	PDH	FH	SA	SL	LL	NRS Back	NRS Leg	JOA	SF36
ADH	1	R=0.660 <i>P=0.001†</i>	R=0.556 <i>P=0.004*</i>	R=0.401 <i>P=0.047*</i>	R=0.168 <i>P=0.423</i>	R=0.248 <i>P=0.231</i>	R=0.075 <i>P=0.720</i>	R=-0.177 <i>P=0.396</i>	R=0.402 <i>P=0.046*</i>	R=0.011 <i>P=0.959</i>	R=0.120 <i>P=0.567</i>
MDH		1	R=0.656 <i>P=0.001†</i>	R=0.267 <i>P=0.196</i>	R=-0.157 <i>P=0.454</i>	R=0.304 <i>P=0.139</i>	R=-0.040 <i>P=0.850</i>	R=-0.364 <i>P=0.074</i>	R=0.169 <i>P=0.418</i>	R=-0.167 <i>P=0.426</i>	R=0.376 <i>P=0.064</i>
PDH			1	R=0.449 <i>P=0.024*</i>	R=-0.116 <i>P=0.580</i>	R=0.138 <i>P=0.511</i>	R=-0.061 <i>P=0.773</i>	R=-0.146 <i>P=0.486</i>	R=0.258 <i>P=0.214</i>	R=-0.089 <i>P=0.673</i>	R=0.222 <i>P=0.287</i>
FH				1	R=-0.153 <i>P=0.465</i>	R=0.024 <i>P=0.909</i>	R=-0.172 <i>P=0.410</i>	R=0.188 <i>P=0.367</i>	R=0.476 <i>P=0.016*</i>	R=0.200 <i>P=0.337</i>	R=0.109 <i>P=0.604</i>
SA					1	R=0.427* <i>P=0.033*</i>	R=0.640 <i>P=0.001</i>	-0.102 <i>P=0.627</i>	R=-0.150 <i>P=0.474</i>	R=0.327 <i>P=0.110</i>	R=0.008 <i>P=0.970</i>
SL						1	R=0.478* <i>P=0.016*</i>	R=-0.427 <i>P=0.033*</i>	R=-0.409 <i>P=0.043*</i>	R=-0.217 <i>P=0.298</i>	R=-0.041 <i>P=0.846</i>
LL							1	R=-0.400 <i>P=0.048*</i>	R=-0.094 <i>P=0.654</i>	R=0.112 <i>P=0.595</i>	R=0.135 <i>P=0.520</i>
NRS Back								1	0.288 <i>P=0.162</i>	R=0.229 <i>P=0.271</i>	R=0.045 <i>P=0.831</i>
NRS Leg									1	R=-0.047 <i>P=0.823</i>	R=0.068 <i>P=0.746</i>
JOA										1	R=0.262 <i>P=0.206</i>
SF-36											1

*Statistically significant values at the 0.05 level, by Pearson correlation coefficient.

†Statistically significant values at the 0.001 level, by Pearson correlation coefficient.

Table 4 Modic change and cage subsidence data in different groups

	rhBMP-2	non-rhBMP-2	<i>P</i> value
Modic 0	10	11	0.046
Modic 1	1	2	/
Modic 2	15	12	0.591
Modic 3	1	0	/
Grade 1	0.61±0.23	0.71±0.12	0.295
Grade 2	1.47±0.31	1.76±0.46	0.095
Grade 3	/	3.01±0.00	/

* Statistically significant among groups.

† Values are presented as means ± SD.

Figures

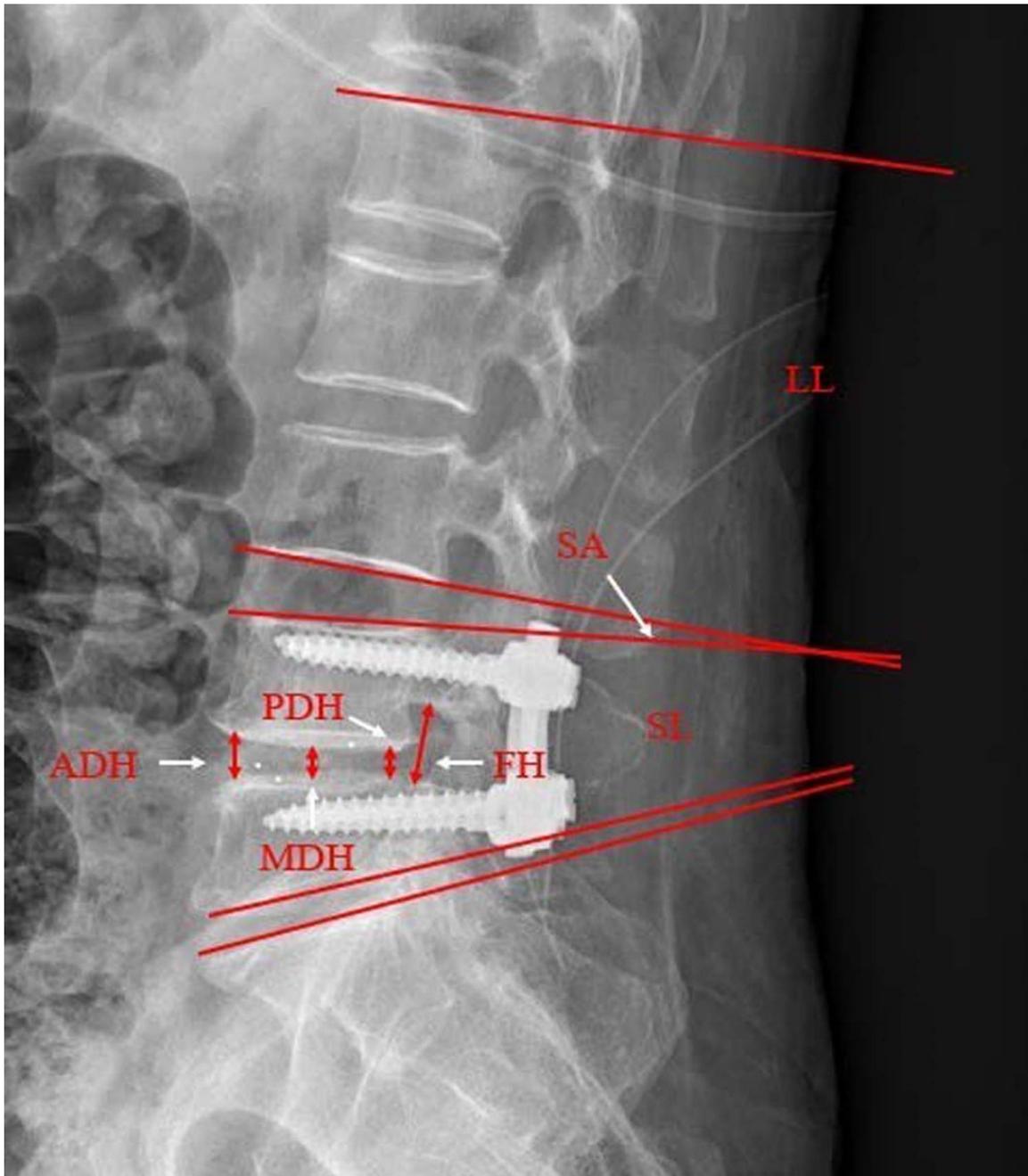


Figure 1

Measurement of sagittal parameters on pre- and postoperative radiographs. Abbreviation: ADH, anterior disc height; MDH, middle disc height; PDH, posterior disc height; FH, foraminal height; SL, segmental lordosis; SA, segmental angle; LL, lumbar lordosis.



Figure 2

Cage subsidence was evaluated by measuring the maximal cranial or caudal migration of the cage into the endplate.

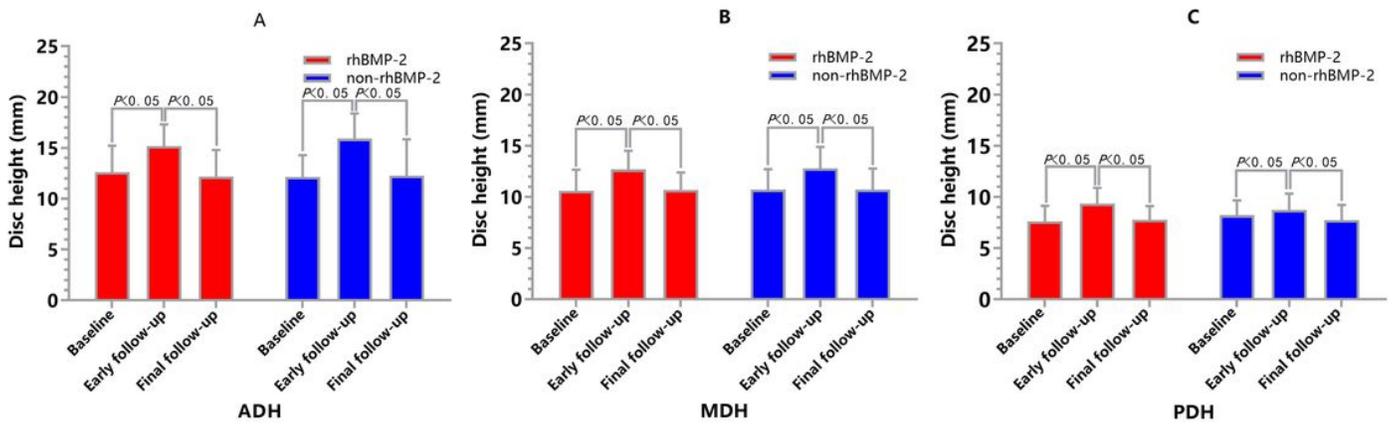


Figure 3

Pre- and postoperative disc height in both groups. Abbreviations: ADH, anterior disc height; MDH, middle disc height; PDH, posterior disc height. Differences are statistically significant if $P < 0.05$.

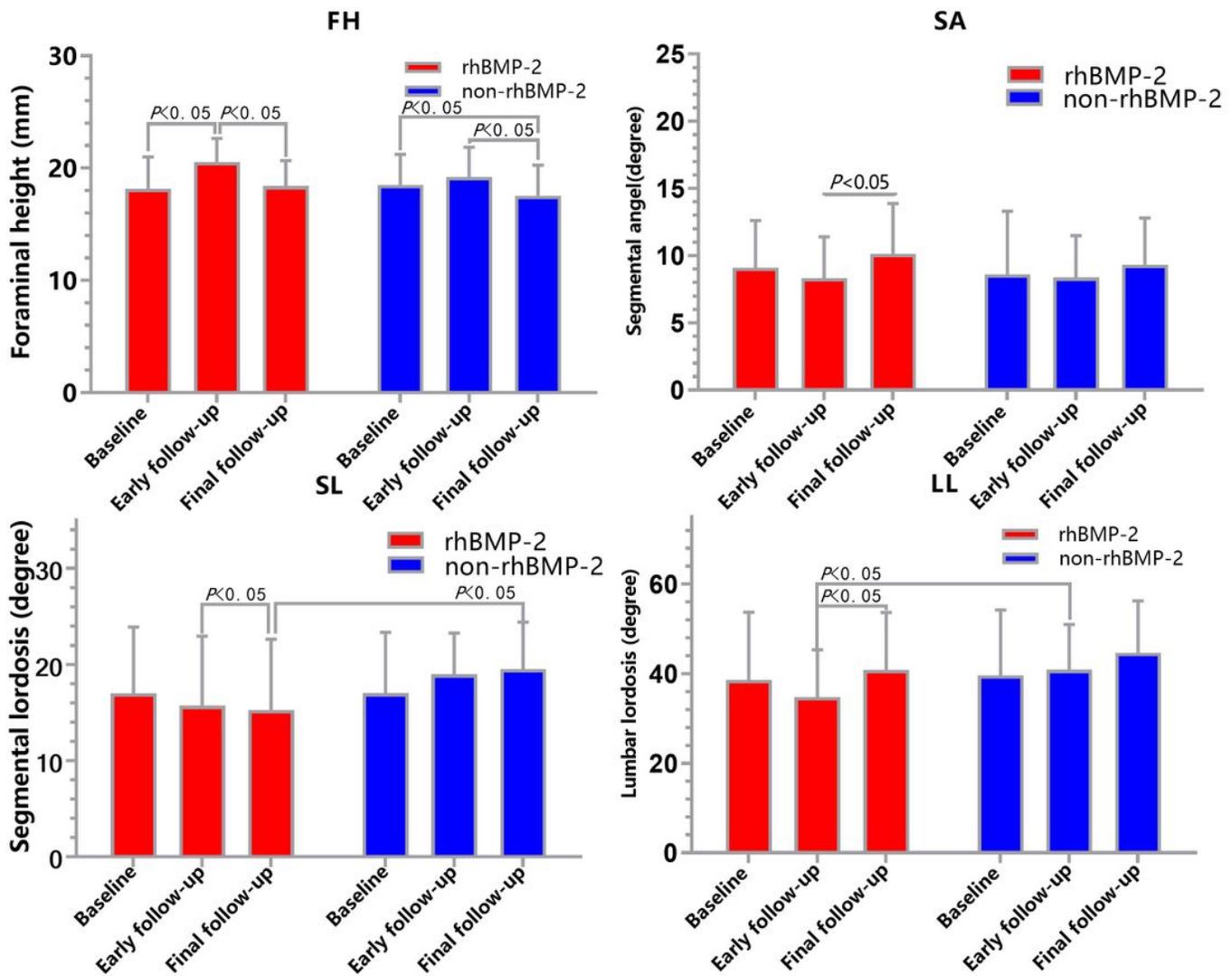


Figure 4

MIS-TLIF combined with or without rhBMP-2 restored foraminal height, segment angle, and segment lordosis in patients with DLD. A: The rhBMP-2 group ($n = 27$) showed a greater improvement in foraminal height during the early follow-up, but the non-rhBMP-2 group ($n = 25$) showed a slight improvement during the early follow-up and restoration in foraminal height in the final follow-up. B: The rhBMP-2 group did not show an improvement in the segment angle. C: The rhBMP-2 group showed a significant improvement in segment lordosis over baseline and the non-rhBMP-2 group in the final follow-up. D: The rhBMP-2 group showed a significant improvement in lumbar lordosis compared to that in the final follow-up and the non-rhBMP-2 group in the early follow-up. Differences are statistically significant if $P < 0.05$.

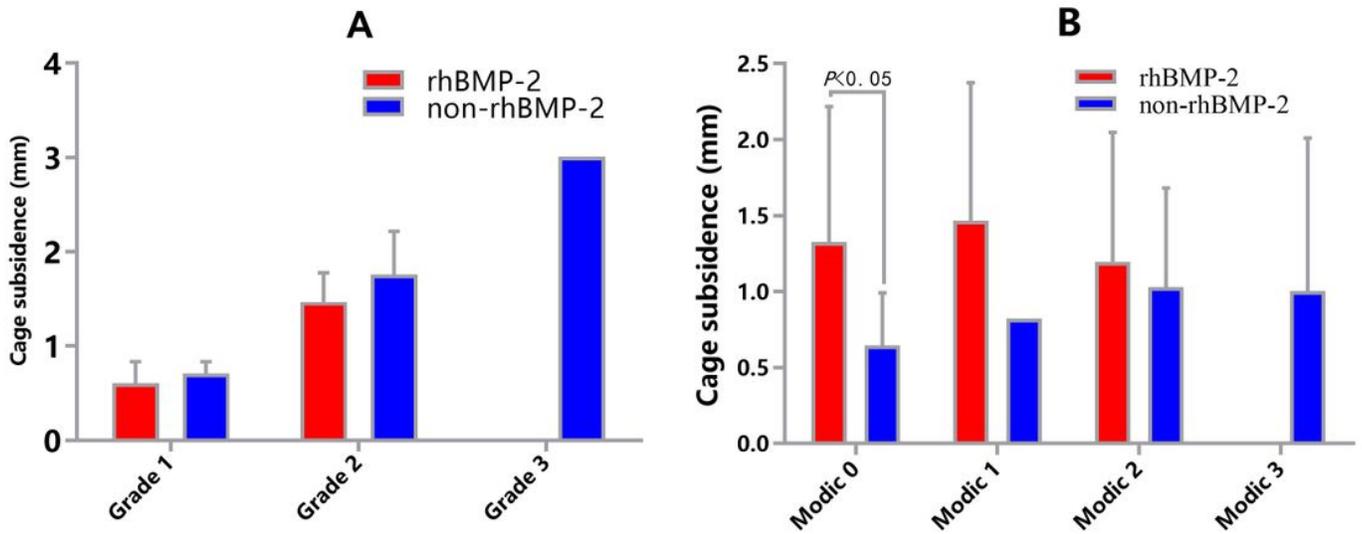


Figure 5

rhBMP-2 had no significant effects on cage subsidence in different cage subsidence groups and modic change groups. rhBMP-2 had no significant effect on cage subsidence grade (A), modic change (B) compared to the non-rhBMP-2 group. Data represent mean \pm SE. Differences are statistically significant if $P < 0.05$.

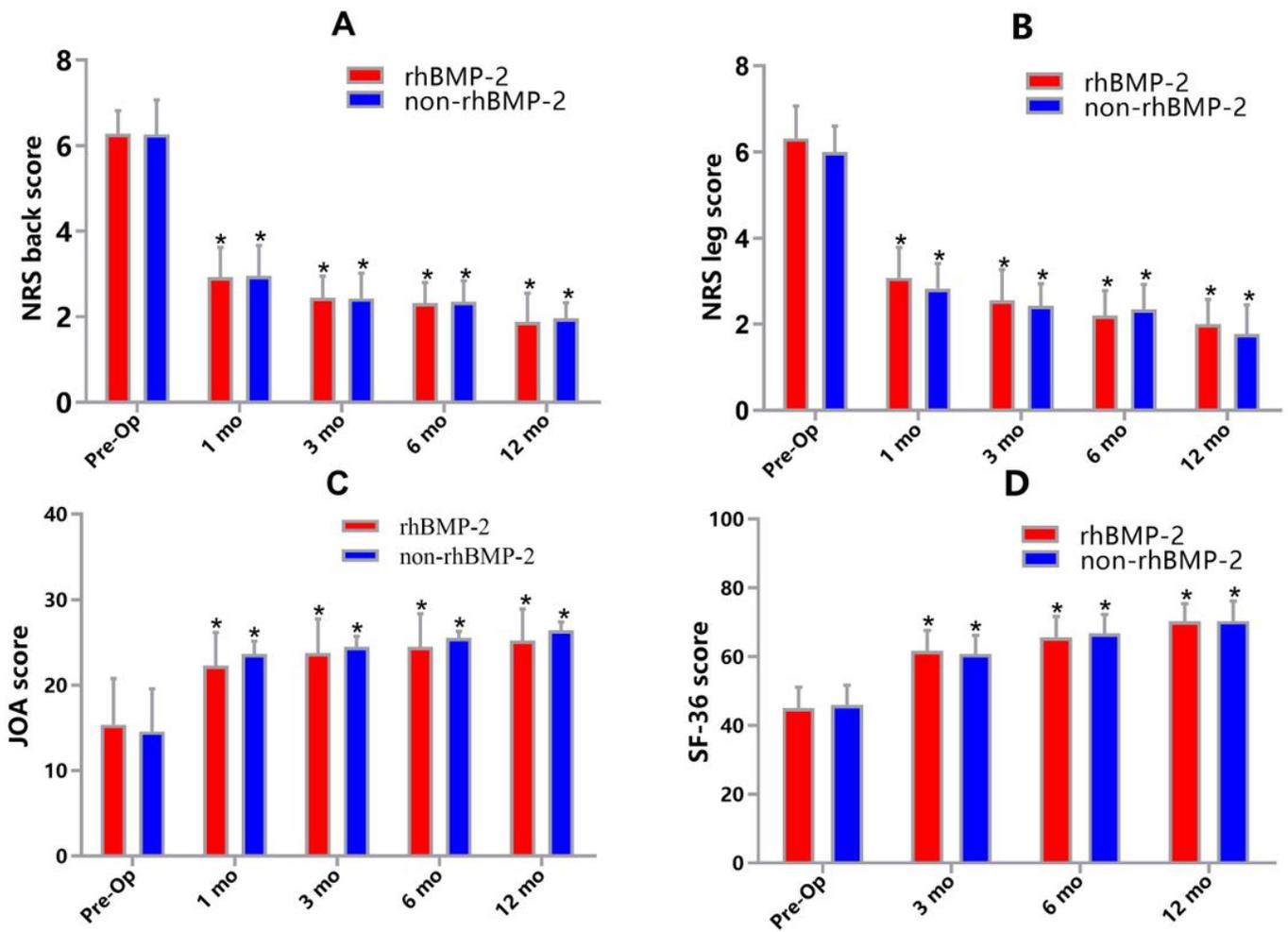


Figure 6

The clinical outcomes of DLD in both groups. rhBMP-2 had no significant effects on the NRS back scores (A), NRS leg scores (B), mJOA scores (C), and SF-36 scores (D) comparing to the scores in the non-rhBMP-2 group. Abbreviation: NRS, numeric rating scale; SF-36, the MOS item short form health survey; JOA, Japanese Orthopedic Association Scores. * indicate statistically significant compared with baseline.