



Heterotopic ossification is related to change in disc space angle after Prestige-LP cervical disc arthroplasty

Lingyun Hu^{1,2} · Jianying Zhang³ · Hao Liu¹ · Yang Meng¹ · Yi Yang¹ · Guangzhou Li¹ · Chen Ding¹ · Beiyu Wang¹

Received: 15 January 2019 / Revised: 25 May 2019 / Accepted: 26 June 2019 / Published online: 5 July 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

Purpose To investigate the influence of the immediate post-operative change in disc space angle relative to preoperation on heterotopic ossification (HO) occurrence following cervical disc arthroplasty (CDA) and on clinical and radiographic outcomes.

Methods Eighty-four patients with single-level Prestige-LP arthroplasty were retrospectively reviewed. HO was assessed based on McAfee classification. Radiological parameters, including index disc space angle (DSA), functional spinal unit angle, cervical lordosis, segmental range of motion (SRM), migration and subsidence of the prosthesis, prosthesis–endplate coverage ratio, and complications, were evaluated. Clinical features and outcome scores were also evaluated.

Results A significant association between immediate post-operative DSA change and HO occurrence was found. Patients with a more than 5° increase in immediate post-operative DSA lordosis had a significantly higher incidence of HO and more severe HO than patients with a less than 5° DSA increase after CDA. No correlation was observed between clinical outcomes and post-operative DSA increase or HO occurrence. Both groups maintained cervical sagittal alignment. However, patients with a more than 5° DSA increase exhibited larger anterior migration amount and lower prosthesis–endplate coverage ratio compared to a less than 5° increase in DSA, and more lordotic DSA and less SRM at the final follow-up compared with those at preoperation. No significant difference in other complications was found between the groups.

Conclusion Patients with a more than 5° increase in immediate post-operative DSA showed adverse effects on HO formation. Overcorrected DSA was associated with poor prosthesis stability, inadequate endplate coverage, and limited SRM, although it did not affect the clinical outcomes.

Graphic abstract

These slides can be retrieved under Electronic Supplementary Material.

Spine Journal
Electronic Supplement
Key points

1. Although maintaining the functional open shell position of the prosthesis and improving local sagittal alignment are important in cervical disc arthroplasty (CDA) surgery, possible changes in local kinematics and stability due to surgical procedures, as well as other risk factors for HO, such as changes in the endplate coverage and in the site and extent of the endplate milling, might affect the occurrence of heterotopic ossification (HO) and the clinical results.
2. The purpose of this study was to investigate the influence of the immediate postoperative change in disc space angle (DSA) relative to pre-operation on HO occurrence following CDA and on clinical and radiographic outcomes, as well as to evaluate its association with important risk factors for HO.

Hu L, Zhang J, Liu H, Meng Y, Yang Y, Li G, Ding C, Wang B (2019) Heterotopic ossification is related to change in disc space angle after Prestige LP cervical disc arthroplasty. *Eur Spine J*.

Spine Journal
Electronic Supplement
Fig. 3 Above, a case showing an increase of less than 5° in immediate postoperative DSA lordosis. Below, a case showing an increase of more than 5° in immediate postoperative DSA lordosis. Lateral radiographs (1) and (2) showed grade I HO and grade 3 HO (arrowheads) at the final follow-up, respectively. The case with more than 5° DSA increase exhibited lower endplate coverage (3) and greater anterior migration (2) compared to the less than 5° increase in DSA (3), (4), and (5), and more lordotic DSA and less SRM (2 and 7) at the final follow-up compared with those at preoperation.

Hu L, Zhang J, Liu H, Meng Y, Yang Y, Li G, Ding C, Wang B (2019) Heterotopic ossification is related to change in disc space angle after Prestige LP cervical disc arthroplasty. *Eur Spine J*.

Spine Journal
Electronic Supplement
Take Home Messages

1. Patients with a more than 5° increase in immediate postoperative DSA lordosis had a significantly higher incidence of HO and more severe HO than patients with a less than 5° DSA increase after Prestige-LP arthroplasty.
2. No correlation was found between clinical outcomes and immediate postoperative DSA increase or HO occurrence.
3. Patients with a more than 5° DSA lordosis increase exhibited larger anterior migration amount and lower prosthesis–endplate coverage ratio compared to a less than 5° increase in DSA, and more lordotic DSA and less SRM at the final follow-up compared with those at pre-operation.
4. An excessive open shell did not significantly increase cervical lordosis, but might increase the complications associated with the prosthesis.

Hu L, Zhang J, Liu H, Meng Y, Yang Y, Li G, Ding C, Wang B (2019) Heterotopic ossification is related to change in disc space angle after Prestige LP cervical disc arthroplasty. *Eur Spine J*.

Keywords Cervical disc arthroplasty · Prestige-LP · Heterotopic ossification · Cohort study · Complications

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00586-019-06053-7>) contains supplementary material, which is available to authorized users.

Extended author information available on the last page of the article

Introduction

As one of the major obstacles of cervical disc arthroplasty (CDA), heterotopic ossification (HO) strongly affects the function of the prosthesis and relief of clinical symptoms in the long term. Moreover, the development of HO abolishes the protective effect of CDA on adjacent segments over time and is associated with the presence of adjacent segment degeneration (ASD) [1, 2]. There is a major discrepancy in the incidence of HO after CDA in different research reports [3], and the precise aetiology of HO after CDA remains unclear. However, surgical technique may be the most important factor affecting HO [4–6].

As an increasingly important factor influencing long-term clinical outcomes, restoration and maintenance of the physiological sagittal alignment and balance are considered essential aspects of a successful CDA [7–10]. However, in contrast to anterior cervical discectomy and fusion, which restores and maintains cervical curvature, sagittal alignment in CDA tends to result in a loss of lordosis due to the prosthetic shell angle, which represents the post-operative disc space angle (DSA), becoming kyphotic after surgery [8, 11]. Some studies have shown that cervical kyphosis after anterior cervical discectomy is associated with the development of clinical adjacent segment disease, axial neck pain, cervical instability, and poor functional recovery [1, 2, 9, 11, 12]. Therefore, to maintain long-term, positive clinical outcomes, maintaining a functional open shell, improving local sagittal alignment, and preventing worsening of segmental kyphosis have recently gained attention in CDA surgery [11–14]. Although most prostheses are not designed to correct kyphosis, sagittal alignment can be improved by modifying techniques, including changing the disc insertion technique and angle, avoiding overmilling of the endplates, and accurately fitting the prosthesis, and these methods show good radiological and clinical results [4, 11, 12, 14].

However, changes to the local alignment and balance during prosthesis implantation might be involved in the occurrence and development of HO; these changes occur through alteration of the biomechanical environment of the cervical spine, as recent studies have suggested that the biomechanical conditions may be related to HO formation following CDA [3, 15–17]. Moreover, changes in endplate procedure in order to maintain a larger open-shell position of the prosthesis might also affect HO. In this study, our aim was to investigate the influence of the immediate post-operative change in index DSA relative to preoperation on the occurrence of HO, as well as its influence on clinical and radiographic outcomes. We hope that this study will provide a theoretical guide for modifying surgical techniques to maintain the long-term outcomes of CDA.

Materials and methods

Patient population

A total of 84 consecutive patients with cervical degenerative disc disease (CDDD) who underwent single-level CDA using a Prestige-LP disc (Medtronic, Memphis, TN, USA) at levels C3/7 between January 2009 and June 2014 in our department were retrospectively reviewed. The study's inclusion criteria for CDA were single-level CDDD between C3/4 and C6/7 in patients with radiculopathy and/or myelopathy who did not respond to conservative treatment for at least 6 weeks or the presence of progressive symptoms of nerve root/spinal cord compression. Computed tomography (CT) and magnetic resonance imaging confirmed spinal cord or nerve root compression. All patients were followed up clinically and radiographically for a minimum of 4 years. The exclusion criteria for CDA included radiographic signs of segmental instability at the index level (defined by translation on flexion–extension radiographs of > 3.5 mm or $> 15^\circ$ angular motion), severe spondylosis (defined by obvious osteophytes, disc height loss of $> 50\%$, or absence of motion [$< 2^\circ$]), incompetent facet joints, ossification of the posterior longitudinal ligament, severe osteoporosis (T -score ≤ -2.5), ankylosing spondylitis, rheumatoid arthritis, cervical infection, diabetes mellitus, pregnancy, metal allergy, neuromuscular disease, and history of cervical spine surgery.

Surgical technique

All operations were performed by the same senior spine surgeon. After general anaesthesia, the patient was placed with the neck in a neutral position, and a standard right-sided anterior cervical approach was used. Complete discectomy and decompression were performed at the index level with removal of the disc tissue, posterior longitudinal ligament, and osteophytes. The endplates and disc space were prepared by using a burr, the trail, Implant Trail and the Rail Cutter Guide. Next, a correctly sized Prestige-LP disc was inserted along with channels in the endplates. Copious irrigation with normal saline was applied to wash away the bone dust when drilling the endplates in every case. After verification of the proper placement and a good match between the vertebral endplate and implant shell through anterior–posterior and lateral fluoroscopy, the incision was closed in a routine manner. After surgery, patients were encouraged to ambulate as early as possible together with physical cervical activities under the guidance of the attending physician and gradually increase the amount of activity.

Outcome assessment

The collected data included patient demographic data, clinical evaluations, and radiographic evaluations. Clinical outcomes were assessed by the visual analogue scale (VAS), Neck Disability Index (NDI), and Japanese Orthopaedic Association (JOA) score. All clinical evaluations were collected preoperatively and at routine post-operative intervals of 3, 6, and 12 months and at the last follow-up.

Radiographic parameters, including cervical lordosis, DSA, functional spinal unit angle (FSUA), and segmental range of motion (SROM), were measured. In this study, we evaluated the preoperative, immediate post-operative (within 1 week), and final follow-up radiographs. Cervical lordosis was calculated using Cobb's angle between the inferior margin of the C2 and C7 vertebral bodies on neutral lateral radiographs; the DSA was defined as the angle formed between the superior and inferior endplate of the index intervertebral space; the FSUA is formed by lines drawn at the superior margin of the superior vertebral body and at the inferior margin of the inferior vertebral body. Lordosis is shown as a positive value, and kyphosis is shown as a negative value. The immediate post-operative change in the DSA relative to preoperation was used as a surrogate measure of the change in DSA (Δ DSA) and was defined as the difference between the preoperative and immediate post-operative DSA values (immediate post-operative value minus the preoperative value). The index DSA lordosis change caused by endplate preparation was defined as the sum of the differences between the superior and inferior endplates of the cephalic and caudal vertebral bodies before and immediately after surgery. The SROM was measured by determining the difference in the DSA between the flexion and extension lateral radiographs. Failure to demonstrate a SROM more than 2° on dynamic radiographs was defined as immobile or loss of arthroplasty function. The prosthesis–endplate coverage ratio was calculated on the median sagittal plane of CT immediately after surgery (calculated by dividing the length of the prosthesis by the length of the endplate) [18]. The presence of HO in the operated segment was evaluated on a cervical X-ray at the final follow-up according to the McAfee classification [19]. Prosthesis stability was investigated by measuring the subsidence and anterior migration of the device [20]. A device was classified as migrated if the anterior migration was > 2 mm or as subsided if the measured subsidence was > 2 mm. Radiographic evidence of ASD was defined by the presence of at least one of the following on radiography: calcification of the anterior longitudinal ligament, a narrowing of the disc space with or without posterior osteophyte, or new anterior or enlarged osteophyte formation [1]. Other complications, including revision surgery, haematoma, or dysphagia, were recorded.

Statistical analysis

Radiographic assessments were performed twice by two independent surgeons, and the mean values were used for statistical analysis. The results are presented as the means \pm standard deviations. The independent *t* test or the nonparametric Mann–Whitney U test were used to compare continuous data between both groups, depending on whether the data were normally distributed or not. Chi-square test or Fisher exact test were used to compare categorical data between the two groups. In each group, comparisons between pre- and post-operative continuous data were performed using the paired sample *t* test or the nonparametric Wilcoxon signed-rank test. Odds ratio with 95% confidence interval was calculated for differences between groups. $p < 0.05$ was considered statistically significant. SPSS software version 20.0 (SPSS, Chicago, IL, USA) was used for statistical analyses.

Results

The patients included 41 men and 43 women, with a mean age of 44.62 ± 7.74 years (27–63). All patients were followed up for at least 48 months, with a mean of 65.16 ± 16.22 months (48–108). The preoperative demographics and post-operative HO occurrence are summarized in Table 1.

Age, sex, preoperative symptoms, involved level, mean length of clinical follow-up, and preoperative SROM were not significantly different for patients with or without HO ($p > 0.05$). In addition, no significant differences were observed in NDI, neck and arm VAS, or JOA scores between patients with HO and without HO ($p > 0.05$). However, in the case of immediate post-operative change in DSA relative to the preoperative value, the result for patients without HO was $3.78^\circ \pm 2.16^\circ$, whereas that of patients with HO was $5.88^\circ \pm 3.96^\circ$; thus, a significant difference was verified ($p = 0.032$) (Table 2).

The mean preoperative DSA at the index level was $1.71 \pm 4.12^\circ$ (-5.55° to 11.08°), and it increased to an immediate post-operative measurement of $6.63^\circ \pm 4.49^\circ$ (-2.90° to 19.52°). The mean change in DSA was $4.92 \pm 3.39^\circ$ (-1.89° to 14.02°). All patients showed an immediate post-operative increase in DSA lordosis, except for two patients who exhibited a decrease in DSA (Δ DSA: -1.89° and -0.30°). The degree of the immediate post-operative change in DSA was divided into Group I (patients with a less than 5° increase in post-operative DSA lordosis, Δ DSA: $2.64^\circ \pm 1.67^\circ$) and Group II (patients with a more than 5° DSA increase, Δ DSA: $8.32^\circ \pm 3.41^\circ$) on the basis of 5° to evaluate the impact of the immediate post-operative change of DSA relative to the preoperative disc angle on

Table 1 Patient demographics and post-operative heterotopic ossification occurrence

Variable	Value
Number of patients	84
Age (years)	44.62 ± 7.74
Sex	
Male	41 (48.8)
Female	43 (51.2)
Follow-up (months)	65.16 ± 16.22
Preoperative symptom	
Radiculopathy	45 (53.6)
Myelopathy	17 (20.2)
Radiculopathy and Myelopathy	22 (26.2)
Levels distribution	
C3/4	1 (1.2)
C4/5	6 (7.1)
C5/6	68 (81.0)
C6/7	9 (10.7)
HO formation	
Grade 1	9 (10.7)
Grade 2	8 (9.5)
Grade 3	11 (13.1)
Grade 4	3 (3.6)
Total	31 (36.9)

HO heterotopic ossification

HO formation. Although a significant difference between the two groups was observed in the index DSA lordosis increase caused by endplate preparation ($1.35^\circ \pm 2.05^\circ$ vs. $4.58^\circ \pm 2.84^\circ$, $p=0.000$) because endplate milling can alter the shell angle of the prosthesis [4, 12–14], the actual lordosis increase in the DSA in Group II was still significantly higher than that in Group I ($3.74^\circ \pm 2.67^\circ$ vs. $1.28^\circ \pm 2.28^\circ$, $p=0.000$).

No significant difference was found in the average age, gender ratio, preoperative symptoms, involved level, or mean length of clinical follow-up between the two groups ($p>0.05$). However, regarding HO formation, the incidence rate of HO in Group I was 27.5%, whereas that in Group II was 51.5%, representing a statistically significant difference ($p=0.026$). In addition, clinically relevant HO (grades 3 and 4) was present in 27.3% of Group II patients and 9.8% of Group I patients ($p=0.036$). Nevertheless, most of the artificial discs in this series remained mobile (overall, 94.0%). Moreover, there were no significant differences in the mobility of prosthesis between the two groups ($p=0.613$) (Table 3, Figs. 1, 2).

For the device stability, the mean amount of subsidence in Group II was slightly larger than that in Group I ($p=0.098$), whereas the mean amount of anterior migration in Group II was significantly larger than that in the latter group ($p=0.000$) (Table 4). Anterior migration of the prosthesis > 2 mm in Group II was radiographically identified

Table 2 Comparison of characteristics of heterotopic ossification formation

Variable	HO (–)	HO (+)	<i>p</i> Value
Number of patients	53	31	
Age (years)	44.29 ± 7.02	44.90 ± 8.47	0.511
Sex (M:F)	28:25	13:18	0.335
Preoperative symptom			0.135
Radiculopathy	31 (58.5)	14 (45.2)	
Myelopathy	12 (22.6)	5 (16.1)	
Radiculopathy and Myelopathy	10 (18.9)	12 (38.7)	
Levels distribution			0.338
C3/4	0 (0)	1 (3.2)	
C4/5	4 (7.5)	2 (6.5)	
C5/6	45 (84.9)	23 (74.2)	
C6/7	4 (7.5)	5 (16.1)	
Follow-up (months)	64.94 ± 16.73	68.85 ± 16.35	0.409
JOA ^a	14.41 ± 1.84	14.70 ± 1.53	0.528
NDI ^a	10.53 ± 3.64	9.65 ± 3.50	0.461
VAS neck ^a	2.06 ± 1.25	2.25 ± 1.12	0.626
VAS arm ^a	2.10 ± 1.30	2.05 ± 1.28	0.984
Preoperative ROM of the index level (°)	10.53 ± 2.19	9.17 ± 2.56	0.144
Immediate post-operative change in DSA (°)	3.78 ± 2.16	5.88 ± 3.96	0.032*

^aEvaluated at the final follow-up

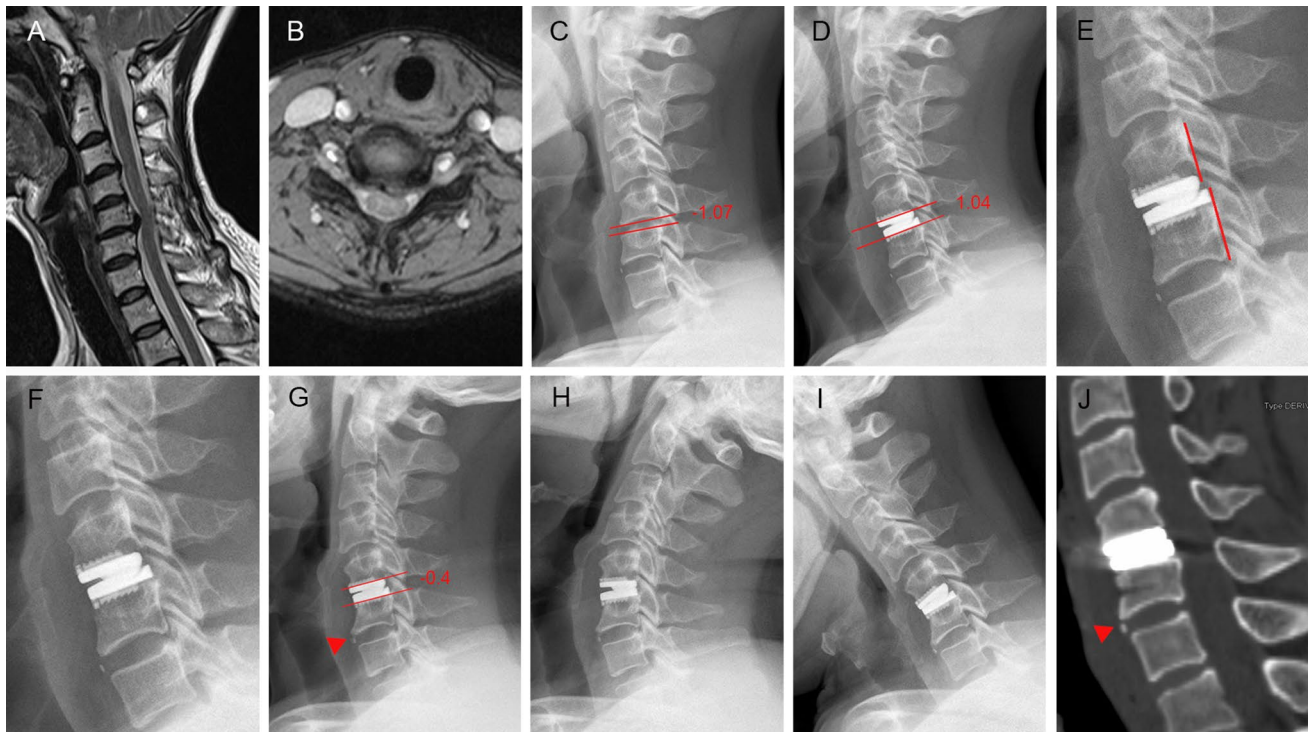
HO heterotopic ossification, JOA Japanese orthopaedic association score, VAS visual analogue scale, NDI neck disability index score, ROM range of motion, DSA disc space angle

* $p<0.05$, statistically significant

Table 3 Comparison of the patient demographics and distribution of heterotopic ossification between the two groups

Variable	Group I ($\leq 5^\circ$)	Group II ($> 5^\circ$)	<i>p</i> Value	Odds ratio
Number of patients	51	33		
Age (years)	46.77 ± 8.01	41.47 ± 6.31	0.083	
Sex (M:F)	29:22	12:21	0.066	
Preoperative symptom			0.955	
Radiculopathy	28 (54.9)	17 (51.5)		
Myelopathy	10 (19.6)	7 (21.2)		
Radiculopathy and Myelopathy	13 (25.5)	9 (27.3)		
Levels distribution			1.000	
C3/4	1 (2.0)	0 (0.0)		
C4/5	4 (7.8)	2 (6.1)		
C5/6	41 (80.4)	27 (81.8)		
C6/7	5 (9.8)	4 (12.1)		
Follow-up (months)	66.73 ± 17.85	64.09 ± 15.36	0.756	
HO (+)	14 (27.5)	17 (51.5)	0.026*	2.81
High-grade HO (\geq grade 3)	5 (9.8)	9 (27.3)	0.036*	3.45
Loss of mobility	2 (3.9)	3 (9.1)	0.613	

HO heterotopic ossification

* $p < 0.05$, statistically significant**Fig. 1** A 40-year-old female who underwent Prestige-LP cervical arthroplasty at C5–6. Preoperative magnetic resonance images (**a**, **b**) showing that disc herniation occurred at C5–6. Preoperative and immediate post-operative lateral radiographs showing 2.11° disc space angle lordosis increase at C5–6 (**c**, **d**). An image with (**e**) and without (**f**) markers showing nicely fitted endplate coverage. Lateral

radiograph (**g**) and CT image (**j**) showed grade 0 heterotopic ossification at 70 months after surgery, with adjacent segment degeneration at the inferior level (C6–7), and anterior enlarged osteophyte formation (arrowheads). Dynamic radiographs (**h**, **i**) demonstrated that the treated level preserved segmental range of motion (10.45°)

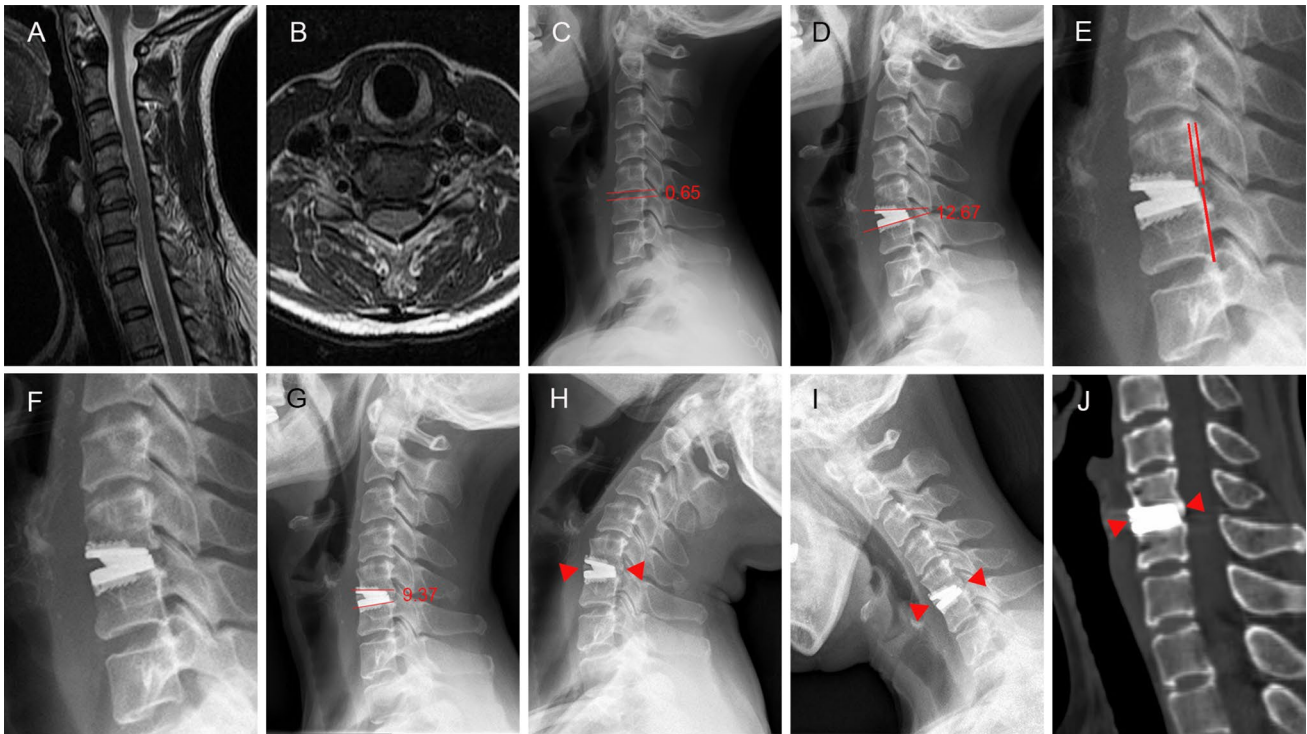


Fig. 2 A 44-year-old male who underwent Prestige-LP cervical arthroplasty at C5–6. Preoperative magnetic resonance images (**a**, **b**) showing that disc herniation occurred at C5–6. Preoperative and immediate post-operative lateral radiographs showing 12.02° disc space angle lordosis increase at C5–6 (**c**, **d**). An image with (**e**) and without (**f**) markers showing inadequate endplate coverage. Lat-

eral radiograph (**g**) and CT image (**j**) showed anterior migration of the prosthesis (2.3 mm) and grade 3 heterotopic ossification (HO) at 57 months after surgery, and dynamic radiographs (**h**, **i**) demonstrated that the implant was stable and the treated level remained mobile (4.5°) despite HO (arrowheads)

Table 4 Comparison of prosthesis stability, prosthesis–endplate coverage ratio, and other complications between the two groups

Variable	Group I (n = 51)	Group II (n = 33)	p Value
Anterior migration (mm)	0.77 ± 0.47	1.23 ± 0.64	0.000*
Migration > 2 mm	1/51	4/33	0.147
Subsidence (mm)	0.57 ± 0.44	0.76 ± 0.63	0.098
Subsidence > 2 mm	0/51	1/33	0.393
Prosthesis–endplate coverage ratio	0.954 ± 0.039	0.915 ± 0.045	0.008*
Radiographic changes at adjacent segments			
New osteophyte formation	4	5	
Osteophyte enlargement	3 ^a	2	
Increased disc space narrowing	1	0	
New disc space narrowing	2 ^a	0	
New or enlarged calcification of the ALL	0	0	
Total	9	7	0.684
Dysphagia	2	1	0.830
Revision surgery	0	0	
Haematoma	0	0	

^aOne of the patients presented with enlarged anterior osteophyte and new narrowing of the disc space

ALL anterior longitudinal ligament

* $p < 0.05$, statistically significant

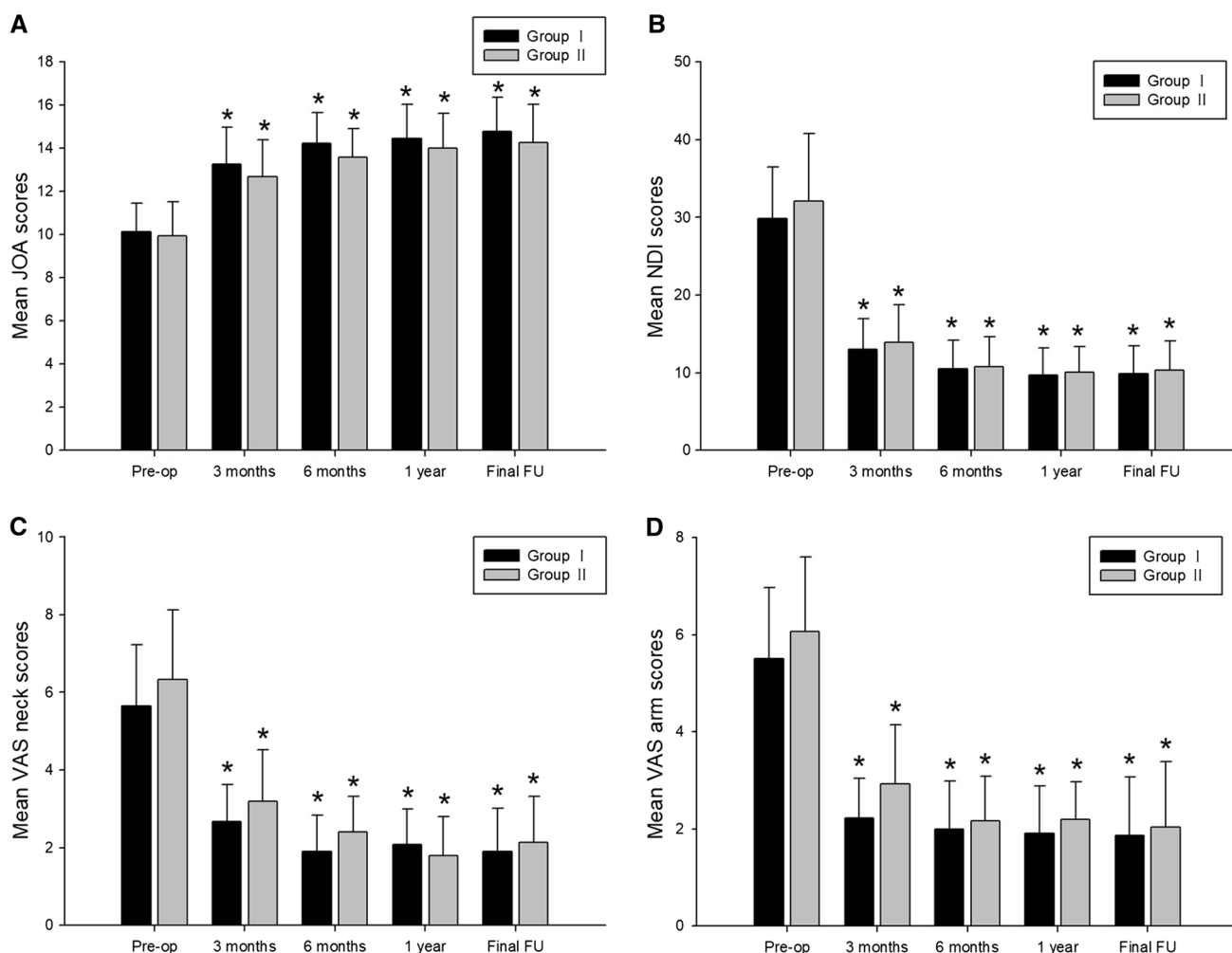


Fig. 3 Clinical outcomes preoperatively and over 4 years of post-operative follow-up. Results are expressed as mean scores \pm SEM at each time point, in Group I (black line) and Group II (grey line). An asterisk represents significant improvement compared with preop-

erative scores. No significant difference was found between the two groups at each time point of evaluation. **a** JOA, **b** NDI, **c** VAS neck, **d** VAS arm

in four patients (12.1%) (Fig. 2) and was higher than that in Group I (1/51, 2.0%), although it was not statistically significant ($p=0.147$) (Table 4). One patient in Group II and no patient in Group I showed prosthesis subsidence > 2 mm ($p=0.393$). However, all the migration and subsidence were stable and required no revision surgery at the last follow-up.

Previous studies demonstrated that inadequate endplate coverage is closely related to HO because the metallic endplate shell may block ectopic bony outgrowth at the edge [5, 18]. We further detected the prosthesis–endplate coverage ratio in the two groups and found that the mean prosthesis–endplate coverage ratio in Group II was significantly lower than that in Group I ($p=0.008$) (Table 4, Figs. 1, 2).

Regarding the clinical outcome, the JOA, NDI, and VAS scores for neck and arm pain at the final follow-up were significantly improved compared with the preoperative scores in both groups ($p < 0.05$). Also, there were no

significant differences between the two groups at each time of evaluation ($p > 0.05$) (Fig. 3).

On average, the preoperative DSA, FSUA, C2-7 angle, and SROM were all comparable between Group I and Group II ($p > 0.05$). At the last follow-up, the mean DSA of Group II was significantly more lordotic than before surgery compared to Group I ($p=0.004$, Fig. 4a). However, no statistical difference in FSUA was found at the last follow-up compared with that at preoperation in both groups ($p > 0.05$, Fig. 4b). Both groups maintained cervical lordosis at the final follow-up assessment, and no significant difference was found between the groups ($p=0.829$) (Fig. 5a). Moreover, the mean SROM in Group II was significantly decreased at the final follow-up compared with that at preoperation ($p=0.046$) and was slightly lower than that in Group I ($p=0.122$) (Fig. 5b).

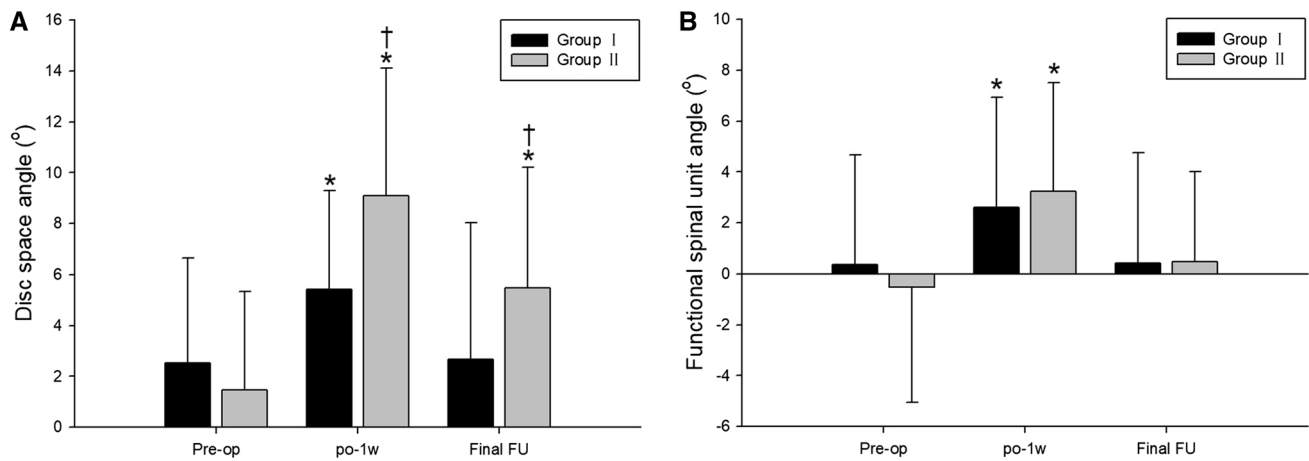


Fig. 4 Comparison of the index disc space angle (a) and functional spinal unit angle (b) in Group I and Group II. Results are expressed as mean ± SEM, in Group I (black line) and Group II (grey line). An

asterisk represents significant difference compared with preoperative values. A sword represents significant difference compared with Group I

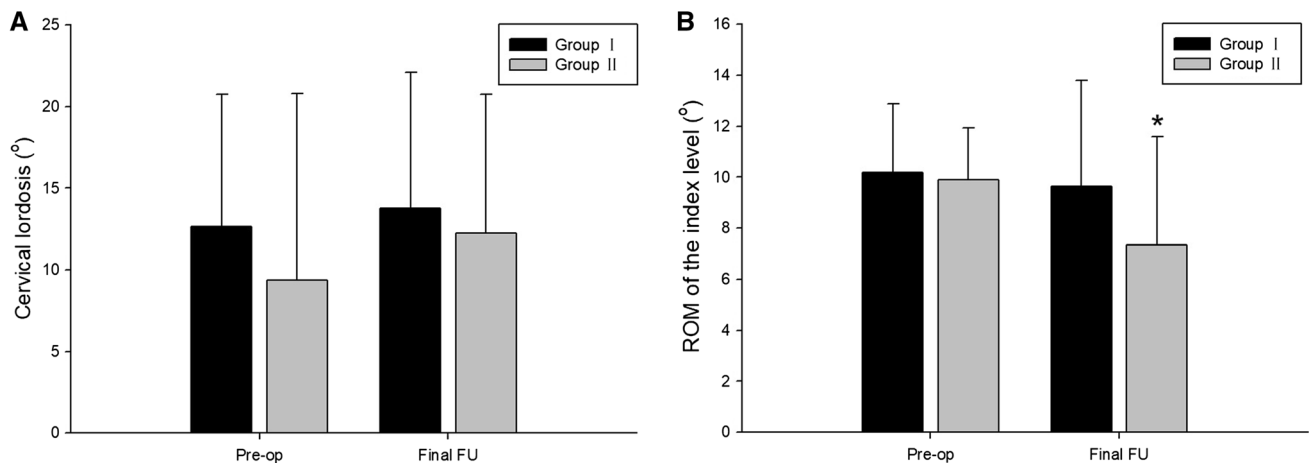


Fig. 5 Comparison of the mean cervical lordosis (a) and range of motion (ROM) of the index level (b) in Group I and Group II. Results are expressed as mean ± SEM, in Group I (black line) and Group II

(grey line). An asterisk represents significant difference compared with preoperative values. No significant difference was observed between the two groups

At the final follow-up, there were no significant differences in the incidence rates of ASD and detectable dysphagia between the two groups after surgery ($p > 0.05$) (Table 4). No patients required secondary surgery because of symptomatic ASD or neurological complications, and all patients with dysphagia recovered during the follow-up. No other complications were found in the present series.

Discussion

Although cervical sagittal alignment is associated with the biomechanical environment and motion pattern of the cervical spine, and may play a substantial role in the development of cervical degeneration [1, 8, 21, 22] and post-operative HO

[15, 17, 23], few studies have focused on the ideal changes in immediate post-operative DSA relative to preoperation required to restore normal kinematics for the index level and to reduce HO occurrence following CDA. Moreover, the degree of correction of DSA is not well addressed in the literature for any of the market-available artificial discs. There is also a lack of consensus regarding specific surgical techniques for disc implantation, even though researchers suggested that insertion of the prosthesis in an unfunctional flexed position should be avoided [4, 5, 11, 12, 14].

The present study showed that the mean immediate post-operative DSA was $6.63^\circ \pm 4.49^\circ$, indicating that Prestige-LP arthroplasty results in an ideal lordosis restoration at the index level close to that of Harrison et al. [24] who found that the average lordosis between cervical vertebrae was

approximately 6° in asymptomatic subjects. In the statistical analysis, the probability that HO formation might occur in the group with a more than 5° increase in immediate post-operative DSA was 51.5%, whereas that in the group with a less than 5°-DSA increase was 27.5%; thus, statistical significance was observed, representing an approximately 2.81 (CI 1.12–7.04) times higher risk in the risk analysis determined by the odds ratio. Meanwhile, based on our observations, the probability that severe HO might occur in the group with a more than 5° DSA lordosis increase was 27.3%, whereas in the group with a less than 5° DSA increase, the probability was 9.8%; thus, statistical significance was observed. This change represents an approximately 3.45 (CI 1.04–11.45) times higher risk in the risk analysis determined by the odds ratio than the risk of patients with a low increase in DSA lordosis. These results indicate that immediate post-operative DSA changes are likely associated with the occurrence and severity of HO.

Several mechanisms may explain the differences in the occurrence and degree of HO between the two groups. Firstly, as mentioned in the literature [4, 12–14], the change in the shell angle is related to bone removal and endplate preparation for the prosthesis. It is important to maintain the open shell of the device by avoiding excessive milling of the posterior part of the bony endplate [4]; meanwhile, relatively more milling the anterior part of the endplate facilitates the prosthesis to maintain a larger open shell [13]. Previous studies suggested that bone exposure during surgical procedure may be a causal factor of HO [6, 15, 23, 25]. This study showed that the index DSA lordosis increase caused by endplate preparation was significantly greater in the high DSA lordosis increase group compared to the low DSA increase group. Therefore, the possible increase in bone resection and bone dusts caused by angled endplate preparation procedure in Group II might be closely related to HO because the anterior part of the lower endplate in the upper vertebra was excessively milled in order to maintain a larger open angle of the Prestige-LP (Fig. 2e, f). Secondly, similar to the recent reports by Lei et al. [13] that overcorrection of local lordosis might increase the risk of anterior migration of the Bryan disc, our results showed that the high DSA lordosis increase also exhibited a larger mean amount of anterior migration compared to the low DSA increase, although the difference in the incidence rate of anterior migration > 2 mm between the groups was not significant. Therefore, this shear stress and instability in the bone–interplant interface induced by higher DSA lordosis increase could be a contributing factor to the formation of HO because Kim et al. [16] indicated that the formation and development of HO may facilitate the restabilization of a biomechanically unstable cervical spine. Moreover, if the DSA is overcorrected, it may result in an increase in significant compression stress and sagittal imbalance in the initial bone–interplant interface, which could

cause microdamage at the prosthesis–bone interface and at the vicinity of the disc footplate; the sustained microdamage activates the coupled action of osteoclasts and osteoblasts to promote bony structural changes, thus promoting HO formation and development. This might also be the main reason why the mean amount of subsidence in Group II was larger than that in Group I, although the difference did not reach statistical significance. Additionally, compared with Group I, inadequate prosthesis–endplate coverage in Group II might be one of the most important reasons for HO formation on the basis of existing relevant investigations [5, 18]. An excessive open shell towards the ventral aspect in the ball-in-trough articulation prosthesis that allows anterior–posterior translation and the possible increase in the endplate depth caused by excessively angled endplate preparation might result in a mismatch between the prosthesis and the endplate, especially for the lower endplate of the cephalic vertebral body. Furthermore, the tendency of anterior migration of the prosthesis might aggravate the mismatch (Fig. 2g).

Some controversial risk factors for HO, such as older age, male sex, operative level, hybrid constructs, and genetic predisposition, have been reported in different studies [15, 17, 23, 25–27]. As shown in our results and previous studies [2, 5, 17, 20, 26], the HO occurrence did not exhibit a significant correlation with age, gender, preoperative symptoms, involved level, clinical outcomes, or preoperative ROM, implying that surgical technique may be the most important factor that affects the development of HO and can also be utilized by a surgeon to prevent HO.

Nevertheless, prosthesis type was shown to influence HO formation [15, 25, 27]. Differences in the design, biomechanical properties, prosthesis-specific end plate articulation component, kinematic performances, and surgical procedure could be contributing factors to HO. In Bryan arthroplasty, the worsening of kyphosis at the index level is significantly higher than other prostheses such as Prestige-LP and Prodisc-C [28], and its post-operative HO incidence rate ranges from 39 to 76.4% over 2 years of follow-up [5, 11, 15, 20]. Some authors also demonstrated that shell kyphosis due to suboptimal carpentry had adverse effects on the formation of HO and segmental mobility after Bryan or Prestige-LP arthroplasty [4, 5]. Although modified surgical techniques can prevent worsening of shell kyphosis and improve local alignment [4, 11, 12, 14], its clinical significance in reducing HO remains unclear. Previous studies have shown that ProDisc-C with a fixed axis of rotation performs better than Bryan and Prestige-LP in maintaining DSA or FSUA lordosis [9, 28]. However, its incidence rate of HO (71.4–90%, over 20 months of follow-up) seems to be significantly higher than that of a prosthesis with a mobile centre of rotation [2, 23, 25, 27], as the latter may better match the physiological motion pattern of the spinal segment and avoid excessive stress concentration at the prosthesis–bone

interface. Meanwhile, keeling procedure leading to excessive removal of bone may also be associated with the high incidence rate of HO [25, 27]. Therefore, in the absence of artificial discs that fully mimic natural cervical disc, it may be necessary to investigate the influence of DSA changes on cervical kinematics and post-operative complications according to prosthesis type, thereby modifying the techniques to improve long-term clinical outcomes.

With regard to clinical outcome, we found no statistically significant differences in the clinical outcome scores between the two groups at the final follow-up, suggesting that the differences in the immediate post-operative increase in DSA lordosis did not affect clinical outcomes in the current series of patients. Similarly, Tu et al. [5] reported that no significant differences were observed in the clinical outcomes between patients with post-operative shell kyphosis and those without shell kyphosis after Bryan arthroplasty. Suchomel et al. [7] and Xu et al. [14] also reported that high lordotic correction did not influence the clinical outcome after Activ C™ or Bryan arthroplasty. These results imply that the relief of clinical symptoms is dependent on thorough neurological decompression during the operation. However, NDI and neck VAS scores could be adversely affected if overcorrecting local lordosis results in anterior migration of the prosthesis after CDA [13].

For the radiographic outcome, the cervical lordosis, DSA, and FSUA were well maintained at the final follow-up in both groups. Compared with Group I, Group II had a significant increase in DSA relative to that at preoperation at the final follow-up because the DSA immediately post-operative was more lordotic in Group II than in Group I. As for the FSUA, we observed no statistical difference at the final follow-up compared with at preoperation in both groups. We speculated that this difference could be corrected within the FSU after minor movement induced by hyperlordotic position [13]. Additionally, relative overmilling of the anterior part of the lower endplate in the upper vertebra and relief of clinical symptoms might also contribute to no significant difference in post-operative FSUA between the groups. We found that the changes in the immediate post-operative DSA did not influence the global alignment, which might be due to the compensatory effect of adjacent segments [12, 13] and the self-adjustment of FSU. Yi et al. [12] and Sasso et al. [21] also demonstrated that there was no significant association between the change in treatment level disc angle and the change in global lordosis.

However, our study showed that the SROM in Group II was significantly reduced at the final follow-up compared to Group I. Rabin et al. [22] demonstrated that there was a significant negative association between DSA and ROM from neutral to extension. We speculated that an excessive open shell would limit ROM, especially in backward extension, because the shells almost touch each other posteriorly [13].

Furthermore, severe HO may adversely affect the SROM at the final follow-up, while Chen et al. [4] showed that restricted ROM may also contribute to the development of HO. In addition, our results demonstrated that the extent of post-operative DSA lordosis increase did not significantly influence the presence of ASD at the final follow-up. Although the development of HO and the low ROM were significantly associated with the development of ASD [1, 2], Lee et al. [1] found an increased lordosis angulation in the angles at the above and operated segments for non-ASD patients. Therefore, long-term follow-up is needed to determine the association between the DSA lordosis increase and the presence of ASD.

The present study, for the first time, demonstrated the influence of the immediate post-operative change in DSA on the formation of HO, and it is not recommended to maintain an excessive open shell in CDA for the HO prevention. However, there are limitations to our study. First, the retrospective nature of our study may be associated with bias. Second, this study only included arthroplasty with Prestige-LP disc and a relatively small number of patients; thus, statistical power was limited. In addition, the occurrence of HO is usually multifactorial. To clarify the current results, a specific study design with multivariate analysis of large-scale and longer follow-up would be important.

Conclusion

Patients with more than a 5° increase in immediate post-operative DSA lordosis showed adverse effects on the formation of HO after Prestige-LP arthroplasty. Overcorrected DSA was associated with poor prosthesis stability, inadequate endplate coverage, and limited SROM, although it did not affect the clinical outcomes. Appropriately correcting DSA may be the more important factor in preventing HO formation and in the long-term success after CDA.

Acknowledgements We thank Dr. Junfeng Zeng MD for his excellent assistance in collecting radiographs and related data. We also thank Drs. Zhiwei Guo and Tingkui Wu for their assistance and helpful suggestions for the statistical analysis.

Compliance with ethical standards

Conflict of interest None of the authors have any potential conflict of interest.

References

1. Lee SE, Jahng TA, Kim HJ (2015) Correlation between cervical lordosis and adjacent segment pathology after anterior cervical spinal surgery. *Eur Spine J* 24:2899–2909. <https://doi.org/10.1007/s00586-015-4132-6>

2. Mehren C, Heider F, Siepe CJ, Zillner B, Kothe R, Korge A, Mayer HM (2017) Clinical and radiological outcome at 10 years of follow-up after total cervical disc replacement. *Eur Spine J* 26:2441–2449. <https://doi.org/10.1007/s00586-017-5204-6>
3. Ganbat D, Kim YH, Kim K, Jin YJ, Park WM (2016) Effect of mechanical loading on heterotopic ossification in cervical total disc replacement: a three-dimensional finite element analysis. *Bio-mech Model Mechanobiol* 15:1191–1199. <https://doi.org/10.1007/s10237-015-0752-3>
4. Chen F, Yang J, Ni B, Guo Q, Lu X, Xie N (2013) Clinical and radiological follow-up of single-level Prestige LP cervical disc replacement. *Arch Orthop Trauma Surg* 133:473–480. <https://doi.org/10.1007/s00402-013-1689-6>
5. Tu TH, Wu JC, Huang WC, Wu CL, Ko CC, Cheng H (2012) The effects of carpentry on heterotopic ossification and mobility in cervical arthroplasty: determination by computed tomography with a minimum 2-year follow-up: clinical article. *J Neurosurg Spine* 16:601–609. <https://doi.org/10.3171/2012.3.SPINE11436>
6. Park JH, Rhim SC, Roh SW (2013) Mid-term follow-up of clinical and radiologic outcomes in cervical total disc replacement (Mobi-C): incidence of heterotopic ossification and risk factors. *J Spinal Disord Tech* 26:141–145. <https://doi.org/10.1097/BSD.0b013e31823ba071>
7. Suchomel P, Jurak L, Antinheimo J, Pohjola J, Stulik J, Meisel HJ, Cabraja M, Woiciechowsky C, Bruchmann B, Shackelford I, Arregui R, Sola S (2014) Does sagittal position of the CTDR-related centre of rotation influence functional outcome? Prospective 2-year follow-up analysis. *Eur Spine J* 23:1124–1134. <https://doi.org/10.1007/s00586-014-3223-0>
8. Di Martino A, Papalia R, Albo E, Cortesi L, Denaro L, Denaro V (2015) Cervical spine alignment in disc arthroplasty: should we change our perspective? *Eur Spine J* 24(Suppl 7):810–825. <https://doi.org/10.1007/s00586-015-4258-6>
9. Yanbin Z, Yu S, Zhongqiang C, Zhongjun L (2011) Sagittal alignment comparison of Bryan disc arthroplasty with ProDisc-C arthroplasty: a prospective, randomized controlled clinical trial. *J Spinal Disord Tech* 24:381–385. <https://doi.org/10.1097/BSD.0b013e318201855f>
10. Chen Y, He Z, Yang H, Wang X, Chen D (2013) Clinical and radiological results of total disc replacement in the cervical spine with preoperative reducible kyphosis. *Int Orthop* 37:463–468. <https://doi.org/10.1007/s00264-012-1754-8>
11. Cao JM, Zhang YZ, Shen Y, Ding WY (2010) Complications of Bryan cervical disc replacement. *Orthop Surg* 2:86–93. <https://doi.org/10.1111/j.1757-7861.2010.00069.x>
12. Yi S, Shin HC, Kim KN, Park HK, Jang IT, Yoon DH (2007) Modified techniques to prevent sagittal imbalance after cervical arthroplasty. *Spine* 32:1986–1991. <https://doi.org/10.1097/BRS.0b013e318133fb99>
13. Lei T, Tong T, Miao D, Gao X, Xu J, Zhang D, Shen Y (2017) Anterior migration after Bryan cervical disc arthroplasty: the relationship between hyperlordosis and its impact on clinical outcomes. *World Neurosurg* 101:534–539. <https://doi.org/10.1016/j.wneu.2017.02.071>
14. Xu JX, Zhang YZ, Shen Y, Ding WY (2009) Effect of modified techniques in Bryan cervical disc arthroplasty. *Spine* 34:1012–1017. <https://doi.org/10.1097/BRS.0b013e31819c4a5b>
15. Jin YJ, Park SB, Kim MJ, Kim KJ, Kim HJ (2013) An analysis of heterotopic ossification in cervical disc arthroplasty: a novel morphologic classification of an ossified mass. *Spine J Off J N Am Spine Soc* 13:408–420. <https://doi.org/10.1016/j.spine.2012.11.048>
16. Kim KS, Heo DH (2016) Do postoperative biomechanical changes induce heterotopic ossification after cervical arthroplasty? A 5-year follow-up study. *Clin Spine Surg* 29:E309–E313. <https://doi.org/10.1097/BSD.0000000000000054>
17. Tian W, Han X, Liu B, He D, Lv Y, Yue J (2017) Generation and development of paravertebral ossification in cervical artificial disk replacement: a detailed analytic report using coronal reconstruction CT. *Clin Spine Surg* 30:E179–E188. <https://doi.org/10.1097/BSD.0000000000000044>
18. Zeng J, Liu H, Chen H, Rong X, Meng Y, Yang Y, Deng Y, Ding C (2018) Effect of prosthesis width and depth on heterotopic ossification after cervical disc arthroplasty. *Spine* 44(9):624–628. <https://doi.org/10.1097/BRS.0000000000002915>
19. McAfee PC, Cunningham BW, Devine J, Williams E, Yu-Yahiro J (2003) Classification of heterotopic ossification (HO) in artificial disk replacement. *J Spinal Disord Tech* 16:384–389
20. Walraevens J, Demaerel P, Suetens P, Van Calenberghe F, van Loon J, Vander Sloten J, Goffin J (2010) Longitudinal prospective long-term radiographic follow-up after treatment of single-level cervical disk disease with the Bryan cervical disc. *Neurosurgery* 67:679–687. <https://doi.org/10.1227/01.NEU.0000377039.89725.F3>. (discussion 687)
21. Sasso RC, Metcalf NH, Hipp JA, Wharton ND, Anderson PA (2011) Sagittal alignment after Bryan cervical arthroplasty. *Spine* 36:991–996. <https://doi.org/10.1097/BRS.0b013e3182076d70>
22. Rabin D, Bertagnoli R, Wharton N, Pickett GE, Duggal N (2009) Sagittal balance influences range of motion: an in vivo study with the ProDisc-C. *Spine J Off J N Am Spine Soc* 9:128–133. <https://doi.org/10.1016/j.spinee.2008.01.009>
23. Suchomel P, Jurak L, Benes V 3rd, Brabec R, Bradac O, Elgawhary S (2010) Clinical results and development of heterotopic ossification in total cervical disc replacement during a 4-year follow-up. *Eur Spine J* 19:307–315. <https://doi.org/10.1007/s00586-009-1259-3>
24. Harrison DD, Harrison DE, Janik TJ, Cailliet R, Ferrantelli JR, Haas JW, Holland B (2004) Modeling of the sagittal cervical spine as a method to discriminate hypolordosis: results of elliptical and circular modeling in 72 asymptomatic subjects, 52 acute neck pain subjects, and 70 chronic neck pain subjects. *Spine* 29:2485–2492
25. Yi S, Shin DA, Kim KN, Choi G, Shin HC, Kim KS, Yoon DH (2013) The predisposing factors for the heterotopic ossification after cervical artificial disc replacement. *Spine J Off J N Am Spine Soc* 13:1048–1054. <https://doi.org/10.1016/j.spinee.2013.02.036>
26. Sundseth J, Jacobsen EA, Kolstad F, Sletteberg RO, Nygaard OP, Johnsen LG, Pripp AH, Andresen H, Fredriksli OA, Myrseth E, Zwart JA (2016) Heterotopic ossification and clinical outcome in nonconstrained cervical arthroplasty 2 years after surgery: the Norwegian cervical arthroplasty trial (NORCAT). *Eur Spine J* 25:2271–2278. <https://doi.org/10.1007/s00586-016-4549-6>
27. Yi S, Kim KN, Yang MS, Yang JW, Kim H, Ha Y, Yoon DH, Shin HC (2010) Difference in occurrence of heterotopic ossification according to prosthesis type in the cervical artificial disc replacement. *Spine* 35:1556–1561. <https://doi.org/10.1097/BRS.0b013e3181c6526b>
28. Kowalczyk I, Lazaro BC, Fink M, Rabin D, Duggal N (2011) Analysis of in vivo kinematics of 3 different cervical devices: Bryan disc, ProDisc-C, and Prestige LP disc. *J Neurosurg Spine* 15:630–635. <https://doi.org/10.3171/2011.8.SPINE11273>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Affiliations

Lingyun Hu^{1,2} · Jianying Zhang³ · Hao Liu¹  · Yang Meng¹ · Yi Yang¹ · Guangzhou Li¹ · Chen Ding¹ · Beiyu Wang¹

✉ Hao Liu
liuhaohuaxi@126.com

³ Department of Radiology, Nanchong Central Hospital,
Second Clinical Medical College of North Sichuan Medical
College, No. 97 Renmin South Rd, Nanchong 637000,
Sichuan, China

¹ Department of Orthopedic Surgery, West China
Hospital, Sichuan University, No. 37 Guo Xue Xiang,
Chengdu 610041, Sichuan, China

² Department of Orthopaedic Surgery, Nanchong Central
Hospital, Second Clinical Medical College of North
Sichuan Medical College, No. 97 Renmin South Rd,
Nanchong 637000, Sichuan, China