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Heterotopic Ossification After Prestige-LP Cervical Disc Arthroplasty Is Related to Insufficient Sagittal Coverage of the Endplate By the Prosthesis

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Background: Heterotopic ossification (HO) is a major complication after cervical disc arthroplasty (CDR) that has attracted the attention of spine surgeons. There remains a great deal of controversy regarding the surgical risk factors. The present study investigated the correlation between insufficient sagittal coverage of the prosthesis-endplate and HO after CDR and explored strategies to prevent it.


Material/Methods: We included 73 patients who underwent Prestige-LP arthroplasty. Patients were divided into HO and non-HO groups. Related data, including radiological, clinical information, were collected. HO was graded using the McAfee classification. Analysis was performed to correlate HO to the surgical segmental range of motion (ROM) at last follow-up. To evaluate the insufficient sagittal coverage of the prosthesis-endplate and other factors for developing HO, receiver operating characteristic (ROC) curves were analyzed for insufficient sagittal coverage.

Results: Among 73 patients, 24 patients had HO at the last follow-up (HO incidence: 32.9%). The ROM in the HO group was significantly lower ($P < 0.001$). The insufficient sagittal coverage of the upper and lower prosthesis-endplate, the height of intervertebral space, and the preoperative and postoperative ROM were related to HO ($P < 0.05$). Multivariate logistic regression analysis showed that only insufficient sagittal coverage of the upper prosthesis-endplate was related to HO ($P = 0.023$), and ROC curve analysis revealed that HO was more likely to occur with insufficient sagittal coverage distance ≥ 2.5 mm.

Conclusions: HO after CDR causes a reduction in ROM, the occurrence of which is associated with insufficient sagittal coverage of the prosthesis-endplate. HO was more likely to occur with insufficient sagittal coverage distance ≥ 2.5 mm.

Keywords: **Arthroplasty, Replacement • Cervical Vertebrae • Ossification, Heterotopic**

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Background

The number of patients with cervical degenerative disc disease (DDD) is gradually increasing. Anterior cervical decompression and fusion (ACDF) is the standard surgical technique for the treatment of cervical DDD, but the range of motion of the spine can be lost due to fusion of the operation segments. Moreover, adjacent segment degeneration is accelerated under stress [1,2]. It has been reported that artificial cervical disc replacement (CDR) can preserve the range of motion of the spine and improve patient quality of life to a greater extent than ACDF [3,4]. However, clinical follow-up reports indicate that heterotopic ossification (HO) can occur after CDR, which will limit range of motion (ROM) and can cause fusion of the replacement segment. Thus, the prosthesis activity can be affected, preventing the goal of CDR from being reached [5-8].

Use of Prestige-LP CDR has been reported in many clinical studies, and the treatment effect is satisfactory. However, HO may occur during follow-up. The pathogenesis of HO after CDR is still not completely clear. Some studies have shown that sex, age, BMI, number of treatment levels, and follow-up time are risk factors for HO [9,10]. However, few studies have investigated the potential role of surgical techniques in HO occurrence following CDR. We found that in many patients with HO, the inserted prostheses were shorter than the vertebral endplates and that HO consistently occurred at the posterior edge of the Prestige-LP prosthesis. Furthermore, some studies revealed that high-grade HO was predicted by residual exposed endplate and that HO was more likely to occur at the posterior edge of the prosthesis when the prosthesis did not have sufficient length [11]. Therefore, our study measured sagittal alignment distance from the posterior margin of the prosthesis to the posterior margin of the vertebral endplate to investigate whether insufficient sagittal coverage of the endplate by the prosthesis can induce HO. This distance was identified as a risk factor for HO after CDR. The aims of the present study were: (1) to investigate whether insufficient sagittal coverage of the endplate by the prosthesis is related to the occurrence of HO after Prestige-LP CDR and (2) to explore how much insufficient sagittal coverage distance can cause HO after Prestige-LP CDR.

Material and Methods

This study was approved by the Ethics Committee (No. 2019-180) and conducted according to the principles of the Declaration of Helsinki. All of the participants signed written informed consent forms, providing consent to participate in this study before their data were stored in the hospital database and used for research.

Patient Selection

This study was a single-center, retrospective, case-control study and was conducted from January 2014 to January 2018 at the First Affiliated Hospital of Chongqing Medical University. The medical records of hospitalized patients diagnosed with DDD (from C-3 to C-7) who received Prestige-LP cervical disc arthroplasty treatment (Medtronic Company) in our department were used for this study. The patient inclusion criteria were: (1) patients with a preoperative clinical diagnosis of DDD from C-3 to C-7, age 18-65 years, and refractory to conservative treatment for at least 6 weeks; (2) patients who underwent Prestige-LP cervical disc arthroplasty treatment (Medtronic Company); and (3) follow-up time of more than 12 months. The exclusion criteria were: (1) patients with a previous history of cervical spine surgery and trauma; (2) cervical infection, tumor, severe osteoporosis (T-score ≤ -2.5), severe hypertension, rheumatoid arthritis, ankylosing spondylitis; (3) long-term nonsteroidal anti-inflammatory drug (NSAID) use; and (4) patients with severe spondylosis or facet joint degeneration, or radiographic signs of instability.

Radiographic Analysis

In addition to analysis of the radiologist's reports, radiographic image analysis was performed independently by 2 senior spine surgeons blind to the radiologist's reports from the First Affiliated Hospital of Chongqing Medical University.

Evaluation of HO Formation

Lateral radiographs of the cervical vertebrae were obtained after the operation. HO was divided into 5 grades according to the McAfee classification method [12]: Grade 0, no HO; Grade I, HO not invading the replacement segmental intervertebral space; Grade II, HO invading the segmental intervertebral space but not affecting the prosthesis motion; Grade III, HO invading the segmental intervertebral space and affecting prosthesis motion; and Grade IV, replacement segment fusion. HO was assessed by 2 spine surgeons independently according to the McAfee classification.

Insufficient Sagittal Coverage of the Endplate

Some inserted prostheses were shorter than the endplate. This finding demonstrated insufficient coverage of the endplate in depth. On a lateral radiograph of the cervical spine, the distance from the posterior edge of the lower endplate of the upper vertebral segment to the posterior edge of the prosthesis was measured, which was defined as the upper prosthesis-endplate sagittal distance (**Figure 1A**). The distance from the posterior edge of the upper endplate of the lower vertebral body to the posterior edge of the prosthesis was measured, defined as the lower prosthesis-endplate sagittal distance (**Figure 1B**).

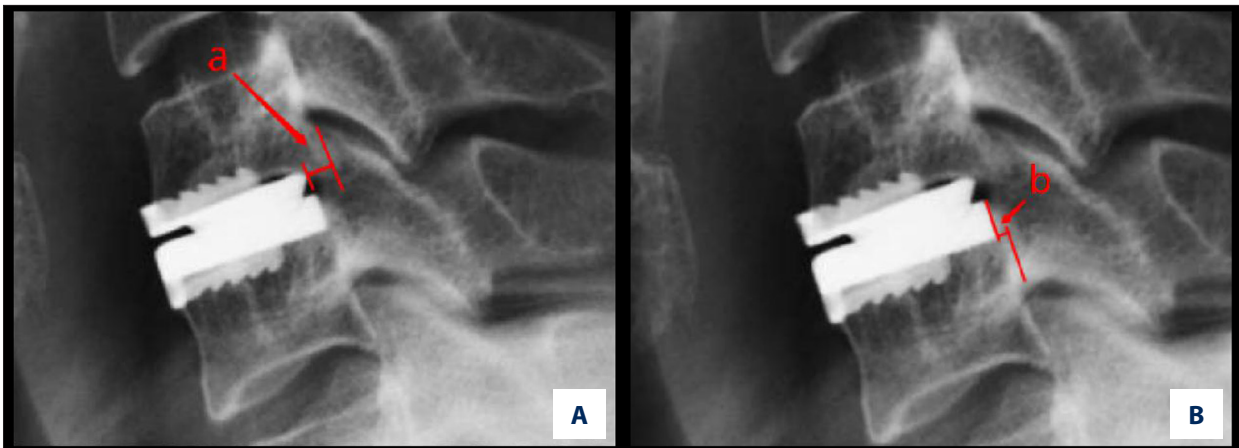


Figure 1. Sagittal alignment accuracy of the prosthesis evaluated by X-ray. This demonstrated that insufficient coverage of the endplate in depth. The upper prosthesis-endplate error distance (A). The lower prosthesis-endplate error distance (B).

These distances were measured to evaluate insufficient sagittal coverage of the measured, defined sagittal alignment error of prosthesis placement.

Preoperative and Postoperative Segmental Range of Motion (ROM)

The White method [13] was used to measure the hyperextension and flexion of the cervical spine on X-ray, and the angle between the posterior edge line of the upper vertebra and the lower vertebra of the surgical segment was measured. The sum of the 2 angles was calculated as the segmental ROM.

Intervertebral Space Height/Adjacent Normal Intervertebral Space Height

The degree of intervertebral disc degeneration was evaluated by measuring the ratio of the height of the surgical segmental intervertebral space to the height of the adjacent normal intervertebral space on the lateral radiograph of the cervical vertebra. The distance between the parallel lines of the upper and lower endplates was calculated as the height of the intervertebral space [5,14].

Surgical Technique

The patients were placed in supine position after general anesthesia, and a C-arm X-ray was used to confirm the lesion segment. The anterior Smith-Robinson approach to the cervical spine was used through a right-sided longitudinal incision with a length of 5-7 cm. A self-retaining retractor was placed over the disc space, and a standard anterior cervical discectomy was performed at the lesion intervertebral level after the position was reconfirmed by a C-arm X-ray. The endplate surfaces were prepared using curettage, and posterior osteophytes were removed using Kerrison rongeurs. Then, the Prestige-LP

prosthesis was implanted at the operative disc level according to the manufacturer's instructions. Finally, C-arm X-ray was used to confirm the position of the prosthesis, and 1 drainage tube was placed in the incision before it was closed layer-by-layer.

Statistical Methods

Data were entered in Microsoft Excel (Microsoft Corporation, Richmond, USA), and statistical analysis was performed using SPSS version 23. Continuous data are expressed as the mean±SD, whereas categorical data are expressed as counts or percentages. Comparison of continuous data were performed utilizing the *t* test, whereas those of categorical data were conducted using the chi-square test. Correlations between variables were investigated by Pearson's correlation coefficient analysis. Based on an exploratory analysis, features believed to have potential relevance to HO were chosen to establish a multivariate logistic regression model. Significant predictors of clinically relevant HO were identified by mixed-effects logistic regression. Receiver operating characteristic (ROC) curve analysis was conducted to determine the extent to which sagittal alignment error can cause HO after CDR. $P < 0.05$ was considered statistically significant.

Results

We included a total of 73 patients who received 12-48 (average 23 months) months of follow-up. HO was experienced by 32% of patients (24/73) after surgery, among whom, 17 patients had single-segment replacement and 7 patients had double-segment replacement. A total of 88 replacement segments were included, of which 25 segments had HO, yielding an incidence rate of 28.4% (25/88). The numbers of HO segments of the different grades were: 1 Grade I, 17 Grade II, 6 Grade III, and 1 Grade IV.

Table 1. Comparison of replacement segment ROM of the HO group and non-HO group at the last follow-up.

	HO		t value	P value
	Have (N=25)	No (N=63)		
ROM of the replacement segment at the last follow-up (°)	3.76~11.08	7.06~13.02	8.493	<0.001

HO – heterotopic ossification; ROM – range of motion. # Compared among the two groups, $P < 0.001$

Table 2. Clinical and imaging features of the included patients.

Index	HO (N=24)	No HO (n=49)	χ^2/t value	P value
Male: Female (n)	12: 12	30: 19	0.831a	0.362
Age (year)	46.25±9.67	47.04±9.08	0.342	0.733
BMI (kg/m ²)	23.40±3.25	23.81±3.57	0.474	0.637
Use NSAIDs: (yes/no) (n)	11: 13	28: 21	0.828a	0.363
Single segment: double segment (n)	17: 7	41: 8	1.627a	0.202
Follow-up time (months)	20.71±10.32	23.96±10.47	1.252	0.764
Nuchal ligament ossification: (yes/no) (n)	7: 17	9: 40	1.098a	0.295
Intervertebral height/adjacent intervertebral height	0.84±0.08	0.88±0.07	2.036	0.046
Preoperative ROM of the replacement segment (°)	5.84±1.09	7.73±1.22	6.423	<0.001
Postoperative ROM of the replacement segments (°)	7.03±1.04	8.85±1.19	6.389	<0.001
The upper prosthesis-endplate sagittal distance (mm)	3.69±0.90	1.88±0.54	-10.706	<0.001
The lower prosthesis-endplate sagittal distance (mm)	1.58±0.81	1.20±0.60	-2.233	0.029

HO – heterotopic ossification; NSAIDs – nonsteroidal anti-inflammatory drugs; ROM – range of motion. # Compared among the two groups: preoperative ROM of the replacement segment, postoperative ROM of the replacement segments, upper prosthesis-endplate sagittal distance ($P < 0.001$), and upper prosthesis-endplate sagittal distance ($P = 0.029$).

Effect of Postoperative HO on the ROM of the Replacement Segment

At the last follow-up, the ROM of the 25 replacement segments in the HO group was 3.76° to 11.08°, and the ROM of the 63 replacement segments in the non-HO group was 7.06° to 13.02°. Results of the *t* test revealed that the displacement degree in the HO group was significantly smaller than that in the non-HO group ($P < 0.001$) (Table 1).

Risk Factors for HO

The following factors were analyzed in the 73 patients: the sagittal distance of the posterior margin of the upper prosthesis endplate, the sagittal distance of the posterior margin of the lower prosthesis endplate, sex, age, BMI, number of replacement segments, preoperative nuchal ligament ossification, ratio of the height of the intervertebral space to the height of the adjacent normal intervertebral space, preoperative and postoperative ROM of the replacement segment, usage of NSAIDs during the perioperative period, and follow-up

time. The following factors were all statistically significant for the HO group ($P < 0.05$): sagittal distance of the posterior margin of the upper prosthesis endplate, sagittal distance of the posterior margin of the lower prosthesis endplate, height of the intervertebral space, and preoperative and postoperative surgical segmental ROM (Table 2). Then, a multilevel statistical model was constructed that included the number of replacement segments and the abovementioned factors with small *P* values. The multivariate logistic analysis showed that only upper prosthesis-endplate sagittal distance was associated with postoperative HO ($P = 0.023$) (Table 3). Therefore, this factor was further analyzed by ROC curve, and the cutoff value was determined by the Youden index. The results showed that patients with a sagittal distance of the posterior margin of the upper prosthesis-endplate ≥ 2.5 mm were more prone to HO (Figure 2). Typical cases are shown in Figures 3 and 4.

Table 3. Multivariate logistic regression analysis.

Index	OR	95% CI LB	95% CI RB	P value
Intervertebral height/adjacent intervertebral height	5.893E-6	5.159E-16	67326.045	0.308
Preoperative ROM of the replacement segment (°)	14.188	0.234	858.611	0.205
Postoperative ROM of the replacement segments (°)	0.576	0.005	68.986	0.821
The upper prosthesis-endplate sagittal distance (mm)	0.000	3.824E-7	0.327	0.023
The lower prosthesis-endplate sagittal distance (mm)	16.598	0.211	1306.906	0.207
Number of replacement segments (n)	0.105	0.001	7.777	0.305

ROM – range of motion. # Indicates a significant interaction between the effect of HO and the upper prosthesis-endplate sagittal distance.

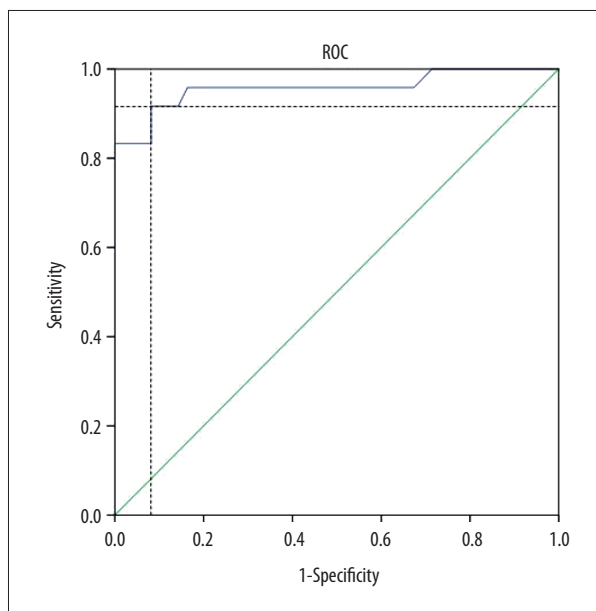


Figure 2. Analysis of how much sagittal alignment error can cause HO by ROC curve analysis. The corresponding variable is 2.5 mm. # Patients with an upper prosthesis-endplate distance ≥ 2.5 mm were more likely to have HO after CDR.

Discussion

In recent years, many studies have found that HO can occur after cervical disc replacement [15–18]. The incidence rate is extremely high, with reports showing rates of 66.2% [17] and 69.6% [18]. Therefore, HO after CDR is a prominent complication that has attracted the attention of surgeons. Our study showed that among the 73 patients who underwent Prestige-LP cervical disc arthroplasty, 24 exhibited HO at the last follow-up, and all HO occurred at the posterior edge of the prosthesis. The incidence rate (32.9%) was similar to that reported by Michael [19] but lower than that reported by Mehran [17]; the differences may result from racial differences, varied choices of surgical indications, and other factors.

The core purpose of CDR is to preserve the displacement of the segmental ROM, and some studies have shown that HO can significantly affect the displacement segmental ROM [20]. However, other studies have found that although the incidence rate of HO is high, Grades III–IV rarely occur, and HO will not have a noticeable effect on the loss of replacement segment ROM during follow-up [21]. Our study showed that at the last follow-up, patients in the HO group had a significantly lower incidence rate of ROM than those in the non-HO group: Grade I: 4% (1/25); Grade II: 68% (17/25); Grade III: 24% (6/25); and Grade IV: 4% (1/25). Some authors reported that HO increases with increasing implantation time of the prosthesis in a long follow-up [22], but our study focused on HO during short-term follow-up, showing that there was no statistically significant difference in follow-up time. Over time, patients with McAfee Grades I–II may have degenerated to Grades III–IV in the follow-up, so the time of HO occurrence and its further development needs long follow-up and further observation.

Although research on HO has surged in recent years, its risk factors are still controversial, and there are a handful of effective strategies to prevent HO after CDR. Different influencing factors have been identified. Pierce [9] showed that sex, obesity, and follow-up time were risk factors for HO after CDR, while Michael [19] and Qi [10] showed that surgical skill proficiency and facet joint degeneration were associated with HO. Nevertheless, HO is a specific complication of CDR, and there is a lack of analytical data for discussing the correlation between CDR surgical factors and postoperative HO. Liu [11] reported that high-grade HO was predicted by residual exposed endplate. Accordingly, we attempted to analyze the influence of surgical factors on HO after CDR by radiographic imaging. We found that during the follow-up, HO of the Prestige-LP cervical disc arthroplasty occurred mostly at the posterior edge of the prosthesis, and follow-up showed that HO was more likely to occur when the prosthesis did not have sufficient length. Therefore, we suggest that HO may be related to the sagittal alignment accuracy of the prosthesis-endplate distance and may be caused by bone contact in the area where the endplate

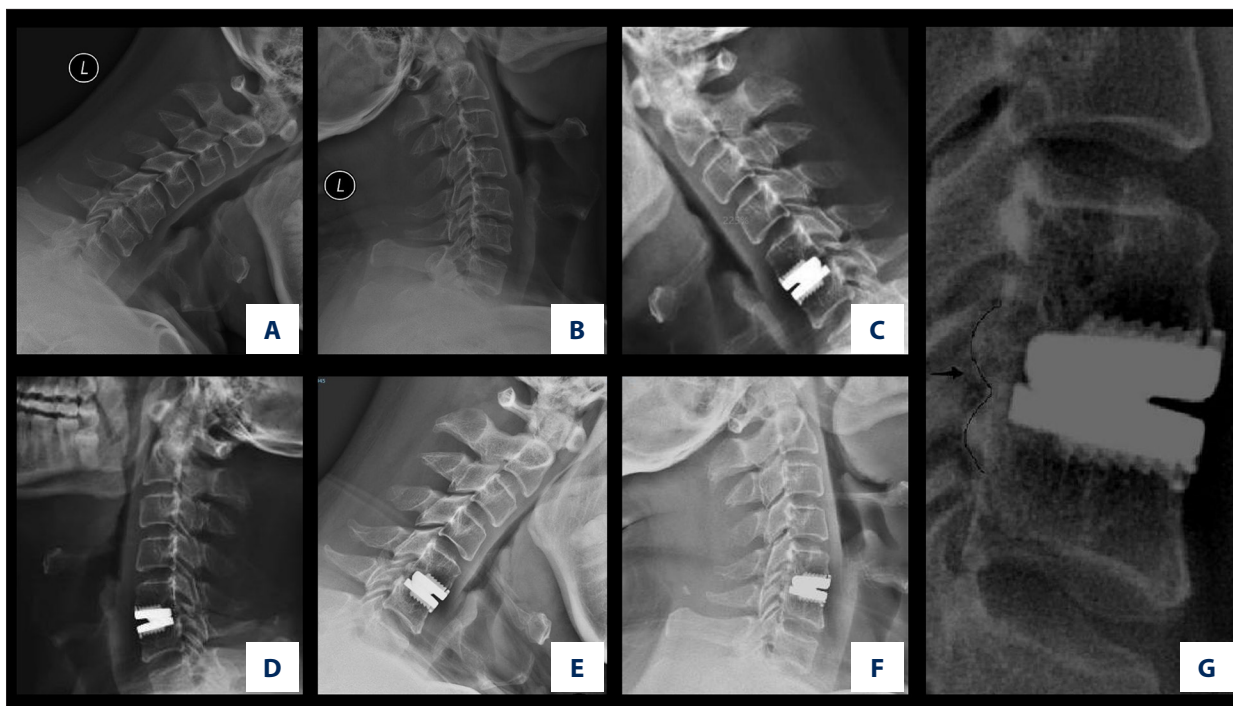


Figure 3. A 51-year-old man with C5/6 Prestige-LP cervical disc arthroplasty. Preoperative flexion and extension roentgenographs indicated that preoperative segmental ROM=4.23° (A, B). Postoperative flexion and extension roentgenographs indicated that postoperative replacement segment ROM=5.9°; the posterior margin of the upper prosthesis-endplate distance was 4.1 mm, and the posterior margin of the lower prosthesis-endplate distance was 2.4 mm (C, D). Postoperative flexion and extension roentgenographs after 36 months indicated that replacement segment ROM=4.39° (E, F), and the postoperative 36-month roentgenograph showed McAfee Grade III HO (G, arrow).

is not covered by the prosthesis. This is a crucial factor that has been ignored, and it could help surgeons prevent postoperative HO after CDR and predict clinical outcomes.

The preliminary analysis showed that the intervertebral height/adjacent intervertebral height, preoperative ROM of the replacement segment, postoperative ROM of the replacement segments, posterior margin of the upper prosthesis-endplate sagittal distance, and posterior margin of the lower prosthesis-endplate sagittal distance were statistically significant. These risk factors are related to exposure of the posterior part of the endplate and movement of the replacement segment. The insufficient coverage in depth can lead to exposure of the posterior part of the endplate. During daily activities, movement of the replacement segment may stimulate the exposed endplate. The repeated stimulation of the exposed endplate may induce inflammation that eventually leads to HO. A study by Liu reported that exposure of the posterior part of the endplate may be associated with HO, but it did not establish a multivariate logistic regression model to analyze nor did it put forward definite strategy to prevent HO after CDR.

Regarding sex, obesity, BMI, and follow-up time, our study found that these risk factors were not statistically significant.

This lack of influence of demographic factors may have been due to the increasingly strict control of CDR indications in patients in recent years. The multivariate regression model analysis results showed that the posterior margin of the upper prosthesis-endplate sagittal distance was an independent risk factor for HO, which confirmed our hypothesis that the sagittal prosthesis-endplate mismatch can lead to HO after CDR.

However, the reasons why only the upper prosthesis-endplate sagittal distance rather than the lower one was statistically significant may be as follows. First, the design of the prosthesis is inappropriate in size. Thaler [23] analyzed several commonly used artificial cervical discs and found that the maximum cover area of the prosthesis was still smaller than that of the vertebral endplate in 53.5% of cases. Additionally, the upper part of the Prestige-LP prosthesis was relatively active, and the lower part was relatively fixed, which resulted in inconsistent coverage of the upper and lower end plates. First, the design of the prosthesis is inappropriate in size. Second, on the sagittal plane, the upper endplate of the lower vertebra is relatively flat. While the lower endplate of the upper vertebra is mostly arched, which is not matched with the commonly used prosthesis endplate [24,25]. Hence, the accuracy of the upper prosthesis-endplate is more prone to sagittal alignment

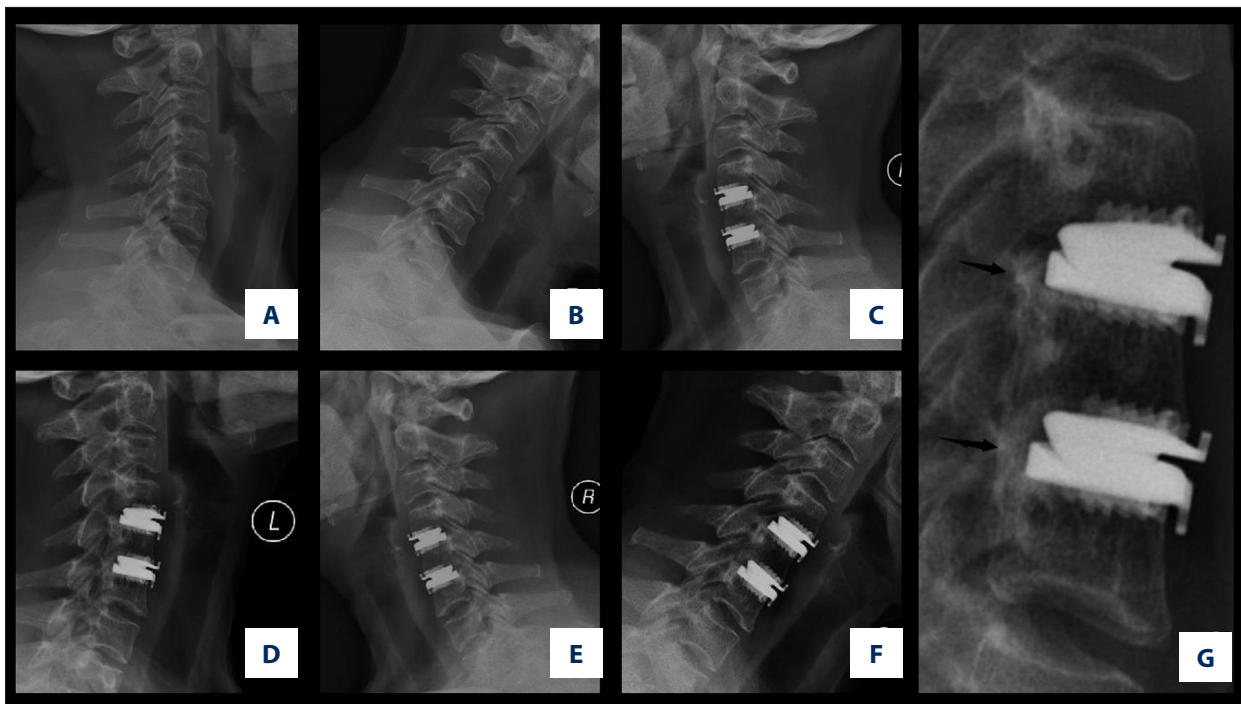


Figure 4. A 52-year-old woman with C4/5 and C5/6 Prestige-LP cervical disc arthroplasty. Preoperative flexion and extension roentgenographs measured the preoperative segmental ROM: C4/5 ROM=6.43°, C5/6 ROM=7.48° (A, B). Postoperative flexion and extension roentgenographs measured the postoperative replacement segment ROM: C4/5 ROM=7.66°, C5/6 ROM=8.07°, posterior margin of the upper prosthesis-endplate distance: C4/5=4.7 mm, C5/6=6.0 mm, posterior margin of the lower prosthesis-endplate distance: C4/5=2.7 mm, C5/6=3.1 mm (C, D). Postoperative flexion and extension roentgenographs after 12 months measured the replacement segment ROM: C4/5 ROM=7.26°, C5/6 ROM=3.76° (E, F), and the postoperative 12-month roentgenograph revealed C4/5 McAfee Grade II HO and C5/6 McAfee Grade III HO (G, arrow).

errors. In the present study, the alignment error of the sagittal distance was consistently higher for the upper prosthesis-endplate than for the lower prosthesis-endplate.

The ROC curves analysis showed that HO was more likely to occur as the sagittal error distance of the prosthesis endplate increased; specifically, HO was more likely to occur with a sagittal error distance ≥ 2.5 mm. This distance has important clinical significance, encouraging greater attention to the sagittal alignment accuracy of prosthesis placement during Prestige-LP cervical disc arthroplasty by intraoperative C-arm fluoroscopic images. It can also serve as a reminder for surgeons to match the anterior-posterior diameter of the prosthesis with the anterior-posterior diameter of the vertebral endplate and to avoid a sagittal error distance of more than 2.5 mm. The computerized 3D measurements of vertebral features can be applied to both normal and pathological cases of anatomy and can aid surgical planning, prosthesis size selection, and the selection of suitable prostheses [26]. Therefore, the use of 3D technology has the potential to help prevent HO.

In addition, clinically, it is considered that the perioperative use of NSAIDs can prevent HO. Our study found no correlation

between the use of NSAIDs and HO, but this relationship needs confirmation by large-sample studies.

Our study has several limitations. First, the sample size was small for a retrospective study. Second, postoperative cervical CT was not routinely performed because of its high cost; thus, only cervical lateral radiographs were analyzed. Third, the effects of different CDR prostheses on HO were not compared. As a result, further studies are required to better assess the risk factors of HO after CDR.

Conclusions

Our results suggest that the accuracy of sagittal alignment of the prosthesis and endplate may be related to the occurrence of HO after Prestige-LP CDR. Insufficient sagittal coverage distance leads to exposure of the posterior part of the endplate, and HO is more likely to occur when the sagittal error distance is more than 2.5 mm. Prestige-LP prostheses should be more precisely inserted to better suit the endplate.

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Conflict of Interest

None.

References:

- Matsumoto M, Okada E, Ichihara D, et al. Anterior cervical decompression and fusion accelerates adjacent segment degeneration: Comparison with asymptomatic volunteers in a ten-year magnetic resonance imaging follow-up study. *Spine (Phila Pa 1976)*, 2010;35(1):36-43
- Yi S, Shin DA, Kim KN, et al. The predisposing factors for the heterotopic ossification after cervical artificial disc replacement. *Spine J*, 2013;13(9):1048-54
- Cason GW, Herkowitz HN. Cervical intervertebral disc replacement. *J Bone Joint Surg Am*, 2013;95(3):279-85
- Pracyk JB, Traynelis VC. Treatment of the painful motion segment: Cervical arthroplasty. *Spine (Phila Pa 1976)*, 2005;30(16 Suppl.):S23-32
- Lee JH, Jung TG, Kim HS, et al. Analysis of the incidence and clinical effect of the heterotopic ossification in a single-level cervical artificial disc replacement. *Spine J*, 2010;10(8):676-82
- Homel P, Jurak L, Benes V, et al. Clinical results and development of heterotopic ossification in total cervical disc replacement during a 4-year follow-up. *Eur Spine J*, 2010;19(2):307-15
- Yi S, Oh J, Choi G, et al. The fate of heterotopic ossification associated with cervical artificial disc replacement. *Spine (Phila Pa 1976)*, 2014;39(25):2078-83
- Leung C, Casey AT, Goffin J, et al. Clinical significance of heterotopic ossification in cervical disc replacement: A prospective multi-center clinical trial. *Neurosurgery*, 2005;57(4):759-63
- Pierce D, Nunley MD, David A, et al. Heterotopic Ossification after cervical total disc replacement at 7 years-prevalence, progression, clinical implications, and risk factors. *Int J Spine Surg*, 2018;12(3):352-61
- Qi M, Chen H, Cao P, et al. Incidence and risk factors analysis of heterotopic ossification after cervical disc replacement. *Chin Med J (Engl)*, 2014;127(22):3871-75
- Zeng J, Liu H, Chen H, et al. Effect of prosthesis width and depth on heterotopic ossification after cervical disc arthroplasty. *Spine J*, 2019;44(9):624-28
- McAfee PC, Cunningham BW, Devine J, et al. Classification of heterotopic ossification (HO) in artificial disk replacement. *J Spinal Disord Tech*, 2003;16(4):384-89
- White AA, Panjabi MM. The basic kinematics of the human spine. A review of past and current knowledge. *Spine (Phila Pa 1976)*. 1978;3(1):12-20
- Homel P, Jurak L, Benes V, et al. Clinical results and development of heterotopic ossification in total cervical disc replacement during a 4-year follow-up. *Eur Spine J*, 2010;19(2):307-15
- Jawahar A, Cavanaugh DA, Kerr EJ, et al. Total disc arthroplasty does not affect the incidence of adjacent segment degeneration in cervical spine: Results of 93 patients in three prospective randomized clinical trials. *Spine J*, 2010;10(12):1043-48
- Sasso RC, Anderson PA, Riew KD, et al. Results of cervical arthroplasty compared with anterior discectomy and fusion: Four-year clinical outcomes in a prospective, randomized controlled trial. *J Bone Joint Surg Am*, 2011;93(18):1684-92
- Mehren C, Suchomel P, Grochulla F, et al. Heterotopic ossification in total cervical artificial disc replacement. *Spine (Phila Pa 1976)*, 2006;31(24):2802-6
- Su Kim K, Hwaheo D. Do postoperative biomechanical changes induce heterotopic ossification after cervical arthroplasty? A 5-year follow-up study. *Clin Spine Surg*, 2016;29(6):E309-13
- Wang MY, Leung CHS, Casey ATH. Cervical arthroplasty with the Bryan Disc. *Neurosurgery*, 2005;56(1 Suppl.):58-65
- Homel P, Jurak L, Benes V, et al. Clinical results and development of heterotopic ossification in total cervical disc replacement during a 4-year follow-up. *Eur Spine J*, 2010;19(2):307-15
- Lee JH, Jung TG, Kim HS, et al. Analysis of the incidence and clinical effect of the heterotopic ossification in a single-level cervical artificial disc replacement. *Spine J*, 2010;10(8):676-82
- Genitiempo M, Perna A, Santagada DA, et al. Single-level Bryan cervical disc arthroplasty: Evaluation of radiological and clinical outcomes after 18 years of follow-up. *Eur Spine J*, 2020;29(11):2823-30
- Thaler M, Hartmann S, Gstottner M, et al. Footprint mismatch in total cervical disc arthroplasty. *Eur Spine J*, 2013;22(4):759-65
- Lakshmanan P, Purushothaman B, Dvorak V, et al. Sagittal endplate morphology of the lower lumbar spine. *Eur Spine J*, 2012;2(Suppl. 2):160-64
- Vander Houwen EB, Baron P, Veldhuizen AG, et al. Geometry of the intervertebral volume and vertebral endplates of the human spine. *Ann Biomed Eng*, 2010;38(1):33-40
- Knez D, Likar B, Pernus F, et al. Computer-assisted screw size and insertion trajectory planning for pedicle screw placement surgery. *IEEE Trans Med Imaging*, 2016;35(6):101-9