CLINICAL ARTICLE

The Assessment of Paravertebral Ossification Progression After Cervical Disc Arthroplasty Based on CT Images: A Long-term Follow-up

Cheng Zeng, MD, Wei Tian, MD, PhD, Bo Liu, MD, Mingxing Fan, MD

Department of Spine Surgery, Beijing Jishuitan Hospital, Beijing, China

Objective: This study focused on the assessment of paravertebral ossification (PO) after cervical disc arthroplasty (CDA) using computed tomography (CT) images.

Methods: In this retrospective study, 52 patients (from 2004 to 2010) who received CDA at a single center were included (32 males). Preoperative and follow-up X-ray and CT images of all patients who underwent single-level CDA were collected. PO from the C2/3 to C7/T1 in each patient was graded based on a CT grading system. Each segment was divided into operative level, adjacent level, or non-adjacent level. The McAfee' classification system was used to grade PO using X-ray plain film. The range of motion (ROM) and scores of neurological symptoms (Japanese Orthopaedic Association [JOA] score and Neck Disability Index [NDI]) at both preoperative and final follow-up time were acquired. Progression and classification of PO in each group was compared using the chi-square test. ROM between groups were compared using independent *t*-test. JOA score and NDI between groups were compared using Mann–Whitney U test.

Results: The average follow-up time was 81.2 months. In comparison with the preoperative status, the progression of PO development in left and right areas (the Luschka joints areas) in the operative level groups was significantly more severe (area L,χ^2 value = 36.612, $P < 0.001$; area R, χ^2 value = 39.172, $P < 0.001$) than the non-adjacent level groups. In contrast, although the prevalence of PO in all areas of the adjacent level groups was higher than that of the non-adjacent level group in the same segments, there was no significant difference ($P > 0.05$) in the progression of PO development. The follow-up high-grade (grades III and IV) PO incidence rate using X-ray grading system (3.85%) was significantly lower than that using CT grading system in area L (42.31%) and R (38.46%), but close to that in area A (5.77%) and P (1.92%). The final follow-up ROM was not significantly different with preoperative ROM in patients with low-grade PO (9.47° ± 4.12° *vs.* 9.76° ± 3.69°, $P = 0.794$). However, in patients with high-grade PO, the final follow-up ROM was significantly lower than preoperative ROM (5.77° ± 3.32° *vs.* 9.28° ± 4.15°, $P < 0.001$). There was no significant difference for JOA score and NDI at follow-up between patients with high-grade and low-grade PO (JOA, 16.2 ± 1.1 *vs.* 16.8 ± 0.9, $P = 0.489$; NDI, 8.9 ± 6.1 *vs.* 8.0 ± 7.3, $P = 0.317$).

Conclusion: High-grade PO was observed in the areas of the Luschka joints at the operative level after CDA, which was difficult to observe using X-ray plain film. The PO formation at adjacent segments was not significant.

Key words: Cervical artificial disc replacement; Cervical disc arthroplasty; Cervical spine; Heterotopic ossification; Paravertebral ossification

Introduction

Cervical disc arthroplasty (CDA) has been a popular surgical technique in recent years. Compared with traditional anterior cervical discectomy and fusion (ACDF), CDA allows some segmental movement and intervertebral disc height to be retained after surgery[1] and therefore

Address for correspondence Wei Tian, MD, PhD, Beijing Jishuitan Hospital, Beijing, China 100035 Tel: 010-58516688; Fax: 010-58516095; Email: drtianweijst@163.com
Received 27 February 2020; accepted 3 June 2020

reduces the incidence of adjacent segment degeneration (ASD)[2–4].

With the increasing use of cervical artificial discs, many researchers have found defects with CDA. Some researchers claim that heterotopic ossification (HO) will occur in the operative segments postoperatively[5, 6]. The existence of HO may cause decreased movement, and even complete fusion, of the operative segments and can trigger ASD postoperatively[1, 7–11], which obviously negates the original purpose of CDA. Tian[6] suggested that HO after CDA surgery is significantly different from traditional HO described for traumatic and joint replacement surgeries. It is difficult to distinguish HO from normal paravertebral osteophyte. Therefore, the type of paravertebral ossification (PO) that includes traditional HO and paravertebral osteophyte was suggested to describe the ossification after CDA.

The influence of CDA on PO formation has been debated by scientists for a long time without agreement. The McAfee classification is the most widely used classification for describing PO[12]. However, using the McAfee classification, the incidence of PO according to different research varies greatly, from 0% to 94.1%[7, 8, 11, 13–16]. The most important reason for this is that the images used for McAfee classification are X-ray plain films, which cannot perfectly show PO on the lateral side of the vertebral body. However, the lateral side of the vertebral body, where the Luschka joints (uncovertebral joints) are located, is a common place for PO formation[6]. Therefore, use of the traditional X-ray image in follow-up to evaluate postoperative HO formation has many limitations[7, 17, 18]. Thus, the actual incidence rate of PO around the Luschka joints might be greatly underestimated due to the popularity of using X-ray plain films in a follow-up.

Unlike plain radiography, computed tomography (CT) can provide a large series of tomographic images, and these cross-sectional slices can be combined into three-dimensional images. Compared with traditional plain X-ray films, CT images have more advantages for the classification and observation of PO. To get a better understanding of PO formation after CDA, it's essential to give a comprehensive assessment of PO using CT images, instead of X-ray plain films. In this study, we used a revised PO grading system based on CT images to assess the prevalence and progression of PO.

PO may also increase with age in the normal cervical spine without surgery as well as in cervical segments that undergo surgery. Therefore, to determine the influence of CDA on PO formation, it's essential to compare the changes in PO in segments that undergo surgery with the changes in segments that do not undergo surgery, instead of discussing whether postoperative PO was larger than preoperative PO. In this study, we assess the differences in PO in different areas of operative, adjacent, and non-adjacent level segments using long-term follow-up, thus assessing the influence of CDA on PO development.

Materials and Methods

Patient Data

In this retrospective study, radiographic data for all patients who underwent single-level CDA using the Bryan disc (Medtronic Sofamor Danek, Memphis, TN, USA) from March 2004 to November 2010 at one hospital were used. All surgeries for selected patients were performed by the same surgical group. Surgeons followed the recommended Bryan artificial cervical disc standard surgery procedures to perform CDA. All patients were asked to ambulate on postoperative day 2 and to wear cervical collar for 2 weeks.

Inclusion criteria were: (i) age more than 18 years, and less than 65 years; and (ii) single-level CDA using the Bryan disc.

Exclusion criteria were: (i) history of previous spine surgery; (ii) multi-level surgery; (iii) cervical instability, spine tumor, infection, fracture, ossification, or calcification of the cervical ligament or history of related diseases; (iv) abnormal metabolism of calcium and phosphorus; and (v) another surgery performed during the postoperative follow-up period.

There were 77 patients who met the inclusion and exclusion criteria in the sample database. Follow-up was completed for 52 patients and the follow-up rate was 67.5%. Cervical lateral and anteroposterior X-ray plain film and CT images of all patients at the final follow-up were collected.

PO Grading System

Preoperative and follow-up CT images were reconstructed into three-dimensional images using Mimics 14.0 (Materialize Interactive Medical Image Control System, Version 14.0; Materialize Corp, Belgium). Per Kouyoumdjian's plan, reconstruction ranged from levels C1 to T2[19]. Thickness was set at 0.5 mm.

A revised CT PO grading system was used to evaluate PO on each segment[9]. With this system, a circle on the horizontal plane of the intervertebral disc in each segment made by the center of the vertebral body was divided into 12 equal clockwise parts (Fig. 1). Area A (anterior) included parts 1, 2, 11, and 12. Area P (posterior) included parts 6 and 7. Area L (left) included parts 3, 4, and 5. Area R (right) included parts 8, 9, and 10. PO grading in each area was evaluated separately (Fig. 2). The grade ranged from 0 to 3.

Two independent, blinded surgeons graded PO based on the revised CT PO grading system from segments C2/3 to C7/T1 in each patient. The X-ray plain films were used to grade PO according to the McAfee classification system[12]. These two surgeons did not participate in the design of the study or the grading system. The grading results of the two surgeons were compared and every difference was discussed by the group to reach an agreement.

Clinical Parameter

Sagittal range of motion (ROM) of the operative segment was calculated at preoperative and final follow-up time using the PACS system (Rogan-Delft, Veenendaal, Netherlands)

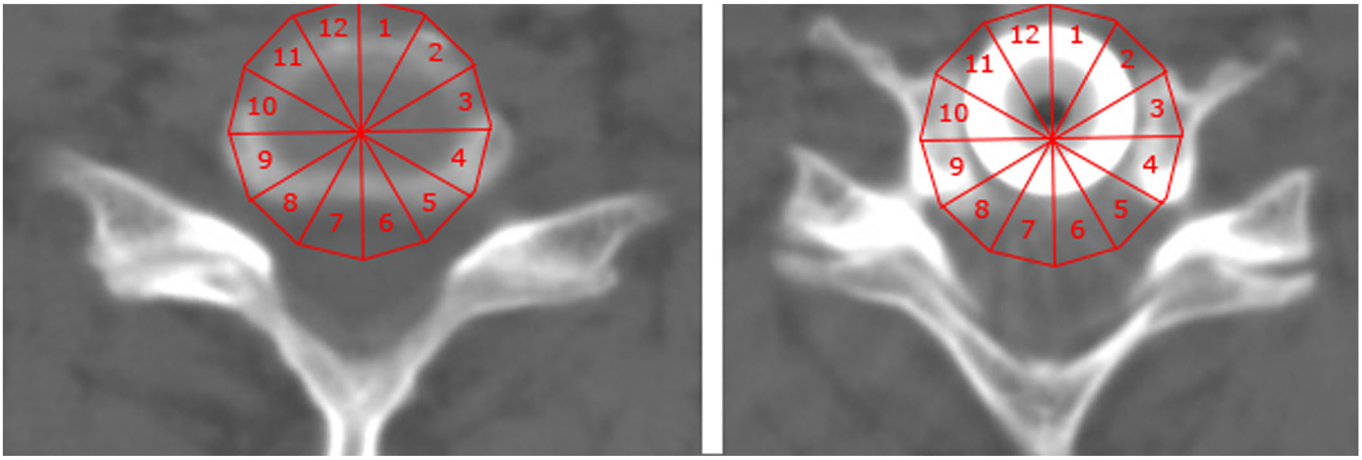

Fig. 1 Suggested areas of the revised CT PO grading system: a circle made in the center of the vertebra body divided into 12 equal clockwise parts. Area A (anterior) includes parts 1, 2, 11, and 12. Area P (posterior) includes parts 6 and 7. Area L (left) includes parts 8, 9, and 10. Area R (right) includes parts 3, 4, and 5.

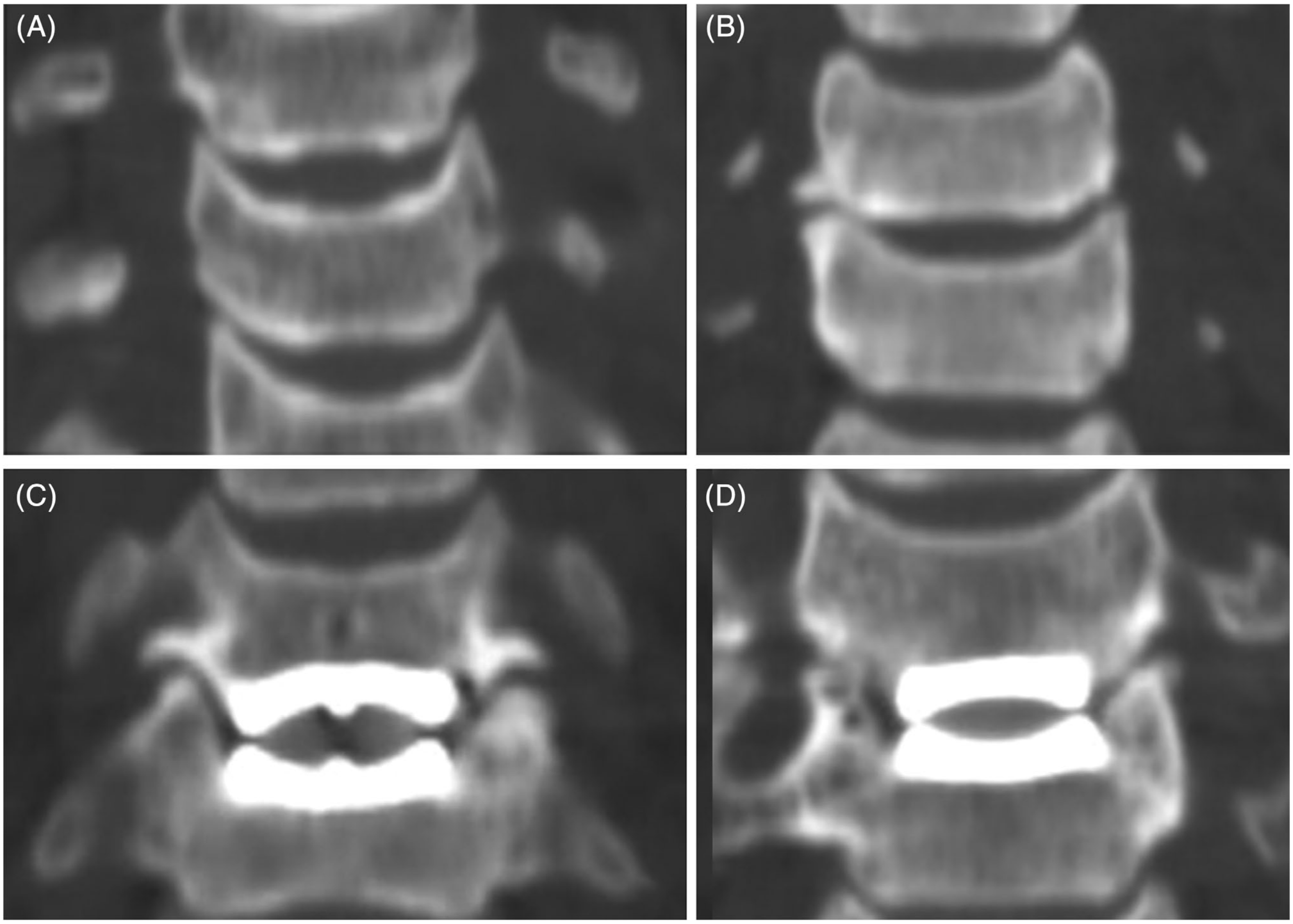

Fig. 2 The revised CT PO grading system: grade 0 (A), no ossification; grade I (B), not extending across the adjacent disc space; grade II (C), extending across the adjacent disc space; and grade III (D), complete bridging of the adjacent disc space.

according to the difference in the Cobb angle between the flexion and extension plain radiographs.

The neural condition at preoperative and follow-up time was evaluated using the Japanese Orthopaedic Association (JOA) score and Neck Disability Index (NDI).

JOA score is for evaluating motor, sensory, and bladder function in patients with cervical myelopathy[4], with a total score of 0 to 17. The higher scores represent better function.

NDI is a self-rated disability score that is composed of 10 questions related to daily activities[4]. The lower scores represent better function.

Statistical Method

Statistical analysis was performed using SPSS 20.0 (Chicago, IL, USA); $P < 0.05$ was considered statistically significant. Each segment was divided into operative, adjacent, or non-adjacent level groups. The non-adjacent level group was considered the normal contrast group. The progression and classification of PO in each group was compared using the chi-square test. Continuous variable data (ROM) which complied with normal distribution, were assessed by p value using independent t-test between groups. Mann–Whitney U test was used for assessing JOA score and NDI which complied with normal distribution between groups. The following subgroup analysis of PO grade at follow-up was made: (i) age < 45 and ≥ 45; (ii) gender; and (iii) follow-up time < 72 months and ≥ 72 months.

Results

General Results

The average age of these 52 patients was 45.6 years (range, 25–56 years). The average follow-up time was 81.2 months (range, 57–108 months). Demographic data are shown in Table 1.

Grading and Distribution of PO

A total of 312 cervical segments of 52 patients were divided into operative, adjacent, or non-adjacent level groups. The non-adjacent level group of one level was considered the normal contrast group of the same level. The PO's CT grading statistics of different groups are shown in Table 2. The postoperative high-grade PO (grades II and III) ratio in every group was higher than that of preoperative high-grade PO. Subgroup analysis of PO grade at follow-up was made according to age, gender and follow-up time. Differences between each subgroup were not significance ($P > 0.05$).

TABLE 1 Demographic data of the patients

Content	Data
Number	52
Average age, years (range)	45.6 (25–56)
Sex	
Male	32
Female	20
Average follow-up time, months (range)	81.2 (57–108)
Surgery level	
C3/4	4
C4/5	9
C5/6	30
C6/7	9

Progression of PO

PO grades from C2/3 to C7/T1 during final follow-up were compared with preoperative grades. If the follow-up grade of an area was higher than its preoperative grade, then it was placed into progressive group. If the PO grade of an area was no different than its preoperative grade, or if PO in this area was excised partially or completely during the surgery, then it was placed into non-progressive group. The segment counts of each group are shown in Table 3. From C3/4 to C6/7, the PO incidence rate of progressive group in the operative levels was significantly higher ($P < 0.05$) than that of the contrast group (non-adjacent levels) in areas L and R. In areas A and P, the PO incidence rate of progressive group in the operative levels was not significantly different ($P > 0.05$) from that of the contrast group. The PO incidence rate of progressive group in the adjacent levels was not significantly different ($P > 0.05$) with that of the contrast group in every area.

Grading of PO Using X-ray Plain Film

The PO grading statistics of operative levels using X-ray plain film according to the McAfee classification system are shown in Table 4. The follow-up high-grade (grade III and IV) PO incidence rate using X-ray grading system (3.85%) was significantly lower than that using CT grading system in area L (42.31%) and R (38.46%), but close to that in area A (5.77%) and P (1.92%).

Clinical Results

In patients with low-grade PO (grade 0, I, and II) at final follow-up, ROM at follow-up was not significantly different with preoperative ROM (9.47° ± 4.12° *vs* 9.76° ± 3.69°, $P = 0.794$), which claimed that ROM was well preserved. But in patients with high-grade PO (grade III) at final follow-up, ROM at follow-up was significantly lower than preoperative ROM (5.77° ± 3.32° *vs* 9.28° ± 4.15°, $P < 0.001$) (Table 5).

The JOA score and NDI at follow-up were significantly improved compared with preoperative scores (JOA: 16.6 ± 0.9 *vs* 13.7 ± 4.6, $P < 0.001$; NDI: 8.2 ± 6.3 *vs* 29.7 ± 14.9, $P < 0.001$). But there was no significant difference for JOA score and NDI at follow-up between patients with high-grade and low-grade PO (JOA, 16.2 ± 1.1 *vs* 16.8 ± 0.9, $P = 0.489$; NDI, 8.9 ± 6.1 *vs* 8.0 ± 7.3, $P = 0.317$).

TABLE 2 PO's CT grading statistics in each area of different groups

Group	Grade	L	R	A	P
Operative level	Pre-op				
	0	16 (30.77%)	20 (38.46%)	25 (48.08%)	14 (26.92%)
	I	14 (26.92%)	16 (30.77%)	16 (30.77%)	14 (26.92%)
	II	22 (42.31%)	15 (28.85%)	8 (15.38%)	23 (44.23%)
	III	0 (0.00%)	1 (1.92%)	3 (5.77%)	1 (1.92%)
	Follow-up				
	0	3 (5.77%)	4 (7.69%)	27 (51.92%)	6 (11.54%)
	I	4 (7.69%)	3 (5.77%)	12 (23.08%)	12 (23.08%)
	II	23 (44.23%)	25 (48.08%)	6 (11.54%)	27 (51.92%)
	III	22 (42.31%)	20 (38.46%)	7 (13.46%)	7 (13.46%)
Adjacent level	Pre-op				
	0	71 (67.80%)	71 (67.80%)	65 (62.71%)	60 (57.63%)
	I	18 (16.95%)	18 (16.95%)	23 (22.03%)	28 (27.12%)
	II	14 (13.56%)	14 (13.56%)	11 (10.17%)	12 (11.86%)
	III	2 (1.69%)	2 (1.69%)	5 (5.08%)	4 (3.39%)
	Follow-up				
	0	51 (49.15%)	55 (52.54%)	44 (42.37%)	33 (32.20%)
	I	23 (22.03%)	18 (16.95%)	28 (27.12%)	37 (35.59%)
	II	28 (27.12%)	28 (27.12%)	21 (20.34%)	25 (23.73%)
	III	2 (1.69%)	4 (3.39%)	11 (10.17%)	9 (8.47%)
Non-adjacent level	Pre-op				
	0	120 (76.83%)	127 (81.71%)	143 (91.46%)	126 (80.49%)
	I	30 (19.51%)	23 (14.63%)	6 (3.66%)	29 (18.29%)
	II	6 (3.66%)	6 (3.66%)	4 (2.44%)	2 (1.22%)
	III	0 (0.00%)	0 (0.00%)	4 (2.44%)	0 (0.00%)
	Follow-up				
	0	88 (56.10%)	107 (68.29%)	114 (73.17%)	82 (52.44%)
	I	38 (24.39%)	29 (18.29%)	21 (13.41%)	53 (34.15%)
	II	29 (18.29%)	15 (9.76%)	13 (8.54%)	21 (13.41%)
	III	2 (1.22%)	6 (3.66%)	8 (4.88%)	0 (0.00%)

TABLE 3 Segment counts in different groups divided by the progression of PO during follow-up

				Contrast			
Group	Area	Progressive	Non-progressive	Progressive	Non-progressive	χ^2 value	*P* value
Operative	L	45 (86.7%)	7 (13.3%)	22 (31.6%)	48 (68.4%)	36.612	0.000*
	R	42 (80.0%)	10 (20.0%)	16 (22.8%)	54 (77.2%)	39.172	0.000*
	A	6 (11.1%)	46 (88.9%)	15 (21.1%)	55 (78.9%)	2.131	0.144
	P	18 (35.5%)	34 (64.5%)	23 (33.3%)	47 (66.7%)	0.064	0.800
Adjacent	L	28 (30.3%)	64 (69.7%)	22 (31.6%)	48 (68.4%)	0.031	0.859
	R	24 (26.3%)	68 (73.7%)	16 (22.8)	54 (77.2%)	0.261	0.609
	A	31 (33.3%)	63 (66.3%)	15 (21.1%)	55 (78.9%)	3.111	0.078
	P	30 (32.9%)	62 (67.1%)	23 (33.3%)	47 (66.7%)	0.003	0.957

[1] *P* < 0.05 (χ^2 test).

TABLE 4 PO's X-ray grading statistics of operative levels

Grade	Pre-op	Follow-up
0	12 (23.08%)	7 (13.46%)
I	14 (26.92%)	15 (28.85%)
II	24 (46.15%)	21 (40.38%)
III%IV	2 (3.85%)	9 (17.31%)

TABLE 5 Comparison of ROM at preoperative and follow-up time (mean ± SD,^{0}), *$P < 0.05$ (independent *t*-test)

	Low-grade (30 levels)	High-grade (22 levels)	All-grade (52 levels)
Preoperative	9.76 ± 3.69	9.28 ± 4.15	9.53 ± 3.86
Follow-up	9.47 ± 4.12	5.77 ± 3.32	7.21 ± 4.19
P-value	0.794	0.000*	0.000*

Discussion

The Underestimated Incident Rate of PO Around the Luschka Joints

One of the advantages of CDA is the preserved postoperative range of segmental motion compared with traditional ACDF. The development of ASD may be slowed or even prevented by acquiring a better postoperative cervical range of motion (ROM). However, the existence of PO may lead to a loss of ROM and, thus, loss of the relative advantage of CDA[20]. In this study, nearly 40% of patients presented with grade III PO during the 7-year follow-up. According to the meta-analysis performed by Chen[21], only 16.7% of patients had high-grade PO during the 2-year follow-up. However, all studies included in Chen's meta-analysis used only plain X-ray films to evaluate the postoperative PO grading. Plain X-ray films, as many researchers agreed[7], are not sensitive enough to evaluate PO grading in the lateral areas, which located near the Luschka joints (uncovertebral joints). In this study, the incidence rate of postoperative PO grade III in areas A and P was 13.46%, which was similar to the meta-analysis results. The difference between the result of X-ray grading and CT grading suggested the same conclusion. Therefore, we have reason to believe that the incidence rate of postoperative PO in the lateral areas was underestimated by former researchers. The most important reason of underestimation was the use of X-ray plain film, which was insufficient to observe the PO located in the lateral area. This study showed that the PO incidence rate using X-ray images was significantly lower than using CT images, especially in the lateral areas. Thus, CT shows great advantage in the follow-up of CDA in this study.

PO and Adjacent Segment Degeneration

In this study, high-grade PO lead to decreased ROM, but no neurological impairment during long-term follow-up. Likewise, according to the meta-analysis performed by Chen[21], PO would lead to decreased postoperative ROM, but not to neurological symptoms. Lee reported that the formation of postoperative PO was significantly relevant to ASD[22]. Thus, the severity of PO in the adjacent segment is one of the evaluation criteria of ASD.

The PO incidence rate is variable at different levels due to the different biomechanical issues. The PO incidence rate in the vertebrae at the same level as the adjacent segment is different from the incidence rate in the vertebrae of a non-surgical non-adjacent segment. The meta-analysis by Zhu[23] reported that CDA resulted in significantly lower postoperative ASD rates than did traditional ACDF. Garrido claimed that the PO incidence rate after CDA was significantly lower than that after ACDF[24]. However, it is unproven whether CDA had an influence on PO development in adjacent levels.

In this study, PO incidence rates and progression rates in adjacent levels were compared with those of non-surgical and non-adjacent levels. Although the PO incidence rate at the adjacent level during final follow-up was higher than that preoperatively, the progression rate was not significantly different between the two groups. Therefore, we speculate that the CDA prosthesis and surgical procedure had no significant influence on PO progression of the adjacent segment. The increasing PO incident rate at the adjacent level could be related to the degeneration reaction during long-term follow-up. However, the CDA itself may not increase the speed of PO formation at the adjacent level.

Hypothesis of PO Formation

Lee[9] claimed that the formation of PO was related to the degenerative inflammatory reaction and that osteophyte formation in the process of degeneration was always accompanied by the formation of PO. Tian[6] claimed that although the original definition of HO was bone formation in ectosteal tissue, 95.2% of HO incidences cited in previous research were not derived from ectosteal tissue, but rather the vertebrae body[6]. It is difficult to distinguish PO caused by postoperative circumstances. According to the study by Yi, the development of PO is a dynamic and continuous process. Unlike traditional HO in limbs, the development of PO does not have a "mature period" 12 months postoperatively. In contrast, PO shows a trend of continuously developing several years after CDA[14]. This indicates that the degeneration reaction has an important role in PO formation and that PO after CDA surgery should be distinguished from traditional HO.

In this study, PO progression in the areas L and R in the operative group was significantly more severe from that of the contrast group, whereas the A and P areas did not show significant differences. Evidence showed that the impact of CDA on PO development is more significant in the lateral areas. In the A and P areas, although the PO level during long-term follow-up was more severe than during the preoperative period, the progression was not significantly different from that in the postoperative normal segment.

The exact cause of PO formation is still unclear. Chalmers claimed that osteogenic cells, induction factors, and a proper environment are required for HO formation[25]. Some researchers surmised that the release of bone morphogenic protein during postoperative or traumatic circumstances played an important role in PO formation[26]. Some researchers claimed that the postoperative residual bone dust was the main cause of PO formation[8, 11, 27]. Therefore, repeated irrigation of the surgical field before disc implant and closure is highly suggested. Nevertheless, bone dust may still be residual in deep parts of the surgical field or behind remaining osteophyte.

Moreover, secondary bone formation reactions after endplate preparation for the Bryan disc implant could be another cause of PO formation[14]. Yi *et al.*[28] suggested that surgical damage of the bone cortex and endplate could lead to PO. With CDA, the bilateral Luschka joints should be kept intact[29]. However, during decompression and prosthesis implantation, it is sometimes difficult to avoid damage of the

Luschka joints. Synder *et al*[29]. suggested that partial excision of the bilateral uncovertebral joints may accelerate osteophyte formation postoperatively. We supposed that the progression of PO in areas L and R in this study was also related to the unexpected cortical injury of the bilateral Luschka joints.

Besides, according to the standard process for Bryan CDA, removal of the osteophytes around the Luschka joints is not strictly required. Therefore, the remaining osteophytes may gradually develop into higher-level PO. Therefore, the strict indications for CDA may be the most important factor for reducing postoperative PO formation. In this study, about two-thirds of the patients had pre-existent low-grade (grade I and II) PO in area L (69.23%) and R (61.54%) at the operative segment. It may be another cause of the high incidence rate of high-grade PO around the Luschka joints in final follow-up. Thus, the choice to keep the osteophytes around the Luschka joints seems to be a dilemma. On the one hand, removal of the osteophyte may inevitably damage the bone cortex of the Luschka joints, and lead to PO formation. On the other hand, the pre-existent PO may also grow to higher-grade PO, and cause ASD in the future. Suggestions still could not be made by the current study, and further research is required.

Limitations

One of the limitations of this study was that only Bryan discs were followed-up. According to the research by Yi, the PO formation rates of Bryan, Mobi-C, and ProDisc-C discs were different[7]. Different artificial discs have different components and designs; therefore, biomechanical features are different. In addition, artificial discs are used in different types of surgical procedures. These differences may influence PO formation[30].

Conclusion

High-grade PO was observed at the operative level after CDA due to long-term follow-up. The progression of PO development at the operative level was concentrated in the areas of the Luschka joints, which was difficult to be observed using plain X-ray film. The influence of CDA on the PO formation at adjacent segments was not significant.

References

1. Heidecke V, Burkert W, Brucke M, Rainov NG. Intervertebral disc replacement for cervical degenerative disease- clinical results and functional outcome at two years in patients implanted with the Bryan cervical disc prosthesis. Acta Neurochir, 2008, 150: 453–459. https://doi.org/10.1007/s00701-008-1552-7.
2. Lei C, Lin N, Li Z, *et al*. Fusion versus Bryan cervical disc in two-level cervical disc disease: a prospective, randomised study. Int Orthop, 2009, 33: 1347–1351. https://doi.org/10.1007/s00264-008-0655-3.
3. Rhee JM. Cervical arthroplasty: a success, failure, or both? Spine J, 2010, 10: 731–732. https://doi.org/10.1016/j.spinee.2010.06.002.
4. Xuesong Z, Xuelian Z, Chao C, *et al*. Randomized, controlled, multicenter, clinical trial comparing BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion in China. Spine, 2012, 37: 433–438. https://doi.org/10.1097/brs.0b013e31822699fa.
5. Demetriades AK, Ringel F, Meyer B. Cervical disc arthroplasty: a critical review and appraisal of the latest available evidence. Adv Tech Stand Neurosurg, 2014, 41: 107–129. https://doi.org/10.1007/978-3-319-01830-0_5.
6. Tian W, Han X, Liu B, He D, Lv Y, Yue J. Generation and development of paravertebral ossification in cervical artificial disc replacement: a detailed analytic report using coronal reconstruction CT. J Spinal Disord Tech, 2013, 30: 179–188. https://doi.org/10.1097/BSD.0000000000000044.
7. Yi S, Kim KN, Yang MS, *et al*. Difference in occurrence of heterotopic ossification according to prosthesis type in the cervical artificial disc replacement. Spine, 2010, 35: 1556–1561. https://doi.org/10.1097/brs.0b013e3181c6526b.
8. Suchomel P, Jurák 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: 307–315. https://doi.org/10.1007/s00586-009-1259-3.
9. Tian W, Fan MX, Liu YJ, *et al*. An analysis of paravertebral ossification in cervical artificial disc replacement: a novel classification based on computed tomography. Orthop Surg, 2016, 8: 440–446. https://doi.org/10.1111/os.12286.
10. Mehren C, Suchomel P, Grochulla F, *et al*. Heterotopic ossification in total cervical artificial disc replacement. Spine, 2006, 31: 2802–2806. https://doi.org/10.1097/01.brs.0000245852.70594.d5.
11. Leung C, Casey AT, Goffin J, *et al*. Clinical significance of heterotopic ossification in cervical disc replacement: a prospective multicenter clinical trial. Neurosurgery, 2005, 57: 759–763; discussion 759-763. https://doi.org/10.1016/j.spinee.2004.05.088.
12. McAfee PC, Cunningham BW, Devine J, *et al*. Classification of heterotopic ossification (HO) in artificial disk replacement. J Spinal Disord Tech, 2003, 16: 384–389. https://doi.org/10.1097/00024720-200308000-00010.
13. Jin HP, Seung CR, Sung WR. Mid-term follow-up of clinical and radiologic outcomes in cervical Total disk replacement (Mobi-C). J Spinal Disord Tech, 2011, 26: 141–145. https://doi.org/10.1097/BSD.0b013e31823ba071.
14. Yi S, Shin DA, Kim KN, *et al*. The predisposing factors for the heterotopic ossification after cervical artificial disc replacement. Spine J, 2013, 13: 1048–1054. https://doi.org/10.1016/j.spinee.2013.02.036.
15. Sasso RC, Best NM, Metcalf NH, Anderson PA. Motion analysis of Bryan cervical disc arthroplasty versus anterior discectomy and fusion: results from a prospective, randomized, multicenter, clinical trial. J Spinal Disord Tech, 2008, 21: 393–399. https://doi.org/10.1097/BSD.0b013e318150d121.
16. Alvin MD, Abbott EE, Lubelski D, *et al*. Cervical arthroplasty: a critical review of the literature. Spine J, 2014, 14: 2231–2245. https://doi.org/10.1016/j.spinee.2014.03.047.
17. Wu JC, Huang WC, Tu TH, *et al*. Differences between soft-disc herniation and spondylosis in cervical arthroplasty: CT-documented heterotopic ossification with minimum 2 years of follow-up. J Neurosurg Spine, 2012, 16: 163–171. https://doi.org/10.3171/2011.10.SPINE11497.
18. Wu JC, Huang WC, Tsai TY, *et al*. Multilevel arthroplasty for cervical spondylosis: more heterotopic ossification at 3 years of follow-up. Spine, 2012, 37: 1251–1259. https://doi.org/10.1097/BRS.0b013e318265a126.
19. Kouyoumdjian P, Bronsard N, Vital JM. Centering of cervical disc replacements: usefulness of intraoperative anteroposterior fluoroscopic guidance to center cervical disc replacements: study on 20 discocerv (scient'x prosthesis). Spine, 2009, 34: 1572–1577. https://doi.org/10.1097/brs.0b013e3181aa1e87.
20. Zhou HH, Qu Y, Dong RP, Kang MY, Zhao JW. Does heterotopic ossification affect the outcomes of cervical total disc replacement? A meta-analysis. Spine, 2015, 40: 332–340. https://doi.org/10.1097/BRS.0000000000000776.
21. Chen J, Wang X, Bai W, Shen X, Yuan W. Prevalence of heterotopic ossification after cervical total disc arthroplasty: a meta-analysis. Eur Spine J, 2012, 21: 674–680. https://doi.org/10.1007/s00586-011-2094-x.
22. Lee SE, Jahng TA, Kim HJ. Correlation between cervical lordosis and adjacent segment pathology after anterior cervical spinal surgery. Eur Spine J, 2015, 24: 2899–2909. https://doi.org/10.1007/s00586-015-4132-6.
23. Zhu Y, Zhang B, Liu H, Wu Y, Zhu Q. Cervical disc arthroplasty versus anterior cervical discectomy and fusion for incidence of symptomatic adjacent segment disease: a meta-analysis of prospective randomized controlled trials. Spine, 2016, 41: 1493–1502. https://doi.org/10.1097/BRS.0000000000001537.
24. Garrido BJ, Wilhite J, Nakano M, *et al*. Adjacent-level cervical ossification after Bryan cervical disc arthroplasty compared with anterior cervical discectomy and fusion. J Bone Joint Surg, 2011, 93: 1185–1189. https://doi.org/10.2106/JBJS.J.00029.
25. Chalmers J, Gray DH, Rush J. Observations on the induction of bone in soft tissues. Bone Joint J, 1975, 57: 36–45. https://doi.org/10.1080/10962247.2013.874380.
26. Ekelund A, Brosjö O, Nilsson OS. Experimental induction of heterotopic bone. Clin Orthop Relat Res, 1991, 263: 102–112. https://doi.org/10.1097/00003086-199102000-00011.

27. Sundseth J, Jacobsen EA, Kolstad F, *et al*. Heterotopic ossification and clinical outcome in nonconstrained cervical arthroplasty 2 years after surgery: the Norwegian cervical arthroplasty trial (NORCAT). Eur Spine J, 2016, 25: 2271–2278. https://doi.org/10.1007/s00586-016-4549-6.
28. Yi S, Oh J, Choi G, *et al*. The fate of heterotopic ossification associated with cervical artificial disc replacement. Spine, 2014, 39: 2078–2083. https://doi.org/10.1097/BRS.0000000000000640.
29. Snyder JT, Tzermiadianos MN, Ghanayem AJ, *et al*. Effect of uncovertebral joint excision on the motion response of the cervical spine after total disc replacement. Spine, 2007, 32: 2965–2969. https://doi.org/10.1097/brs.0b013e31815cd482.
30. Lee JH, Jung TG, Kim HS, Jang JS, Lee SH. Analysis of the incidence and clinical effect of the heterotopic ossification in a single-level cervical artificial disc replacement. The Spine Journal: Official Journal of the North American Spine Society, 2010, 10: 676–682. https://doi.org/10.1016/j.spinee.2010.04.017.