

Original Article

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Received: August 14, 2020 Revised: September 13, 2020 Accepted: September 13, 2020



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Vertebral Endplate Cyst Formation in Relation to Properties of Interbody Cages

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Objective: This retrospective study aimed to compare vertebral endplate cyst formation (VECF), an early predictor for pseudoarthrosis, in different types of interbody cages. Methods: We reviewed 84 cases treated with single-level posterior/transforaminal lumbar interbody fusion. We utilized a polyetheretherketone cage in 20 cases (group P), a titanium cage in 16 cases (group Ti), a titanium-coating polyetheretherketone cage in 13 cases (group TiP) and a porous tantalum cage in 35 cases (group Tn). VECF was evaluated comparing the computed tomography scans taken at day 0 and 6-month postoperation. We defined VECF (+) as enlargement of a pre-existing cyst or de novo formation of a cyst with the diameter over 2 mm. We calculated the adjusted odds ratio (OR) and 95% confidence intervals (CIs) as an indicator of association between different types of cages and VECF using a logistic regression model.

Results: VECF was observed in 13 (65%), 7 (44%), 9 (69%), and 8 (23%) cases in groups P, Ti, TiP and Tn, respectively. VECF correlated with the type of cage (p = 0.04). In comparison with group P, the proportion of VECF (+) cases was lower in group Tn (OR, 0.16; 95% CI, 0.04–0.60) but not different in group Ti (OR, 0.47; 95% CI, 0.10–2.20) and group TiP (OR, 1.06; 95% CI, 0.21-5.28). No patient underwent additional surgery for the fused spinal level during the follow-up periods (average, 37.9 months; range, 6–76 months). Conclusion: VECF was the least in the porous Tn cage, suggesting its potential superiority for initial stability.

Keywords: Vertebral endplate cyst formation, Polyetheretherketone, Titanium, Tantalum, Posterior lumbar interbody fusion, Interbody cage

INTRODUCTION

Posterior lumbar interbody fusion (PLIF) or transforaminal lumbar interbody fusion (TLIF) is a common surgical method used for the treatment of spinal instability or deformity caused by degenerative diseases. Its goal is to gain solid fusion between desired vertebrae of the spine. Interbody cages are usually used for these surgeries, and autologous bone and/or artificial bone material are grafted with cages into the intervertebral space. The cages are expected to support the anterior spinal stability and help in the promotion of arthrodesis. Various types of cages

with different designs and properties have been introduced to improve the fusion rate.

Fujibayashi et al. reported that cyst formation on the vertebral endplate adjacent to interbody cages is a predictor of pseudarthrosis in the early postoperative periods. The authors initially defined the vertebral endplate cyst formation (VECF) as a de novo cyst formation or enlargement of a pre-existing endplate cyst. Later, a diffuse osteolytic defect, which seems identical to periprosthetic osteolysis, was also regarded as VECF.^{2,3} Moreover, 1 case report showed that periprosthetic osteolysis occurred in succession after de novo cyst formation.4 Therefore, VECF

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can be considered as an early stage of endplate osteolysis. Previous studies have shown that periprosthetic osteolysis correlated with pseudarthrosis, ^{5,6} and that VECF including periprosthetic osteolysis is affected by the type of cage. ^{2,5,6} As such, proper selection of the interbody cage is important in preventing VECF and obtaining successful arthrodesis.

In this retrospective study, we compared VECF among 4 types of cages with different properties in order to find a favorable cage for PLIF/TLIF.

MATERIALS AND METHODS

1. Patients and Utilized Cages

We reviewed the clinical records of 142 consecutive cases treated with PLIF/TLIF from April 2013 to May 2019 at Iseikai Hospital. During this time period, resection of cartilage endplate and bone grafting were performed in a consistent manner as described later. We selected patients treated with a singlelevel PLIF/TLIF, excluding cases with adjacent segmental disease or vertebral fracture. As a result, 84 patients were included in this study. Of the 4 types of 22-mm length cages with different properties, we used a polyetheretherketone (PEEK) cage (Capstone-P, Medtronic Sofamor Danek, Memphis, TN, USA) in 20 cases (group P), a titanium (Ti) cage (Capstone-T) in 16 cases (group Ti), a Ti-coated PEEK cage (Capstone-PTC) in 13 cases (group TiP) and a porous tantalum (Tn) cage (TM Ardis, Zimmer Biomet Holdings, Warsaw, IN, USA) in 35 cases (group Tn). The types of cages used were determined not by the surgeon but by our department. Each cage was consistently used in a certain period. This study was approved by the ethics committee of Iseikai Hospital (No. 2019-9) and patients' consent was obtained for the usage of data in this retrospective study.

2. Surgical Methods of Interbody Fusion

In the PLIF procedure, the cartilaginous endplate was carefully removed using raspatriums and curettes without injuring the osseous endplate. A couple of interbody cages were inserted from the bilateral foramen into the intervertebral space. Bone struts and milled bone pieces made from the local bone were grafted between the 2 cages. In the TLIF procedure, the intervertebral disc and the cartilaginous endplate were removed from the unilateral vertebral foramen. One interbody cage was inserted into the intervertebral space and pushed into the contralateral side. Subsequently, bone struts and milled bone pieces were grafted into the intervertebral space and pushed to the medial side. Finally, one more cage was inserted into the ipsilat-

eral side of the intervertebral space.

3. Assessment of Radiological and Clinical Outcomes

The primary outcome of this study was the detection of VECF at 6-month postoperation. Cage subsidence and pain reduction, using visual analogue scale (VAS), were assessed as secondary radiological and clinical outcomes, respectively.

Computed tomography (CT) scan was performed at day 0 and 6-month post-PLIF/TLIF procedures. VECF and cage subsidence was evaluated independently by 2 neurosurgeons (YM and TF). VECF (+) was defined as enlargement of the pre-existing cyst or de novo formation of a cyst with a diameter greater than 2 mm on any corresponding section of the multiplanner reconstruction (MPR) sagittal and coronal images. If one of the evaluators can detect VECF (+), the case was subsequently adjudicated as VECF (+). For evaluation of cage subsidence, the distance between the midpoints on the endplates opposite to the fusion site was measured independently by the 2 observers using the midline section of the MPR sagittal CT images (Fig. 1A, B). In the case of L5-S1 fusion, one of the midpoints was used as the upper end of the S1-2 boundary (Fig. 1C, D). A decrease in the mean distance between the midpoints on the endplates observed at day 0 and 6-month postoperation was calculated in each case. Cage subsidence (+) was defined as a decrease in the mean distance by > 2 mm.

VAS for low back pain (LBP) and leg pain (LP) were recorded at pre-operation and 6-month postoperation. We excluded 4 cases (P: Ti: TiP: Tn = 1: 0: 2: 1) from this clinical outcome, because of the failure in recording preoperative or postoperative VAS. Pain reduction (+) was defined as a postoperative decrease of the VAS by > 20 mm, according to a previous report.⁷

4. Statistical Analysis

We described baseline characteristics of all subjects using the mean and standard deviation (SD) or proportion and percentage. Subsequently, we described the incidence of VECF, cage subsidence and pain reduction and used the Fisher exact method to compare the proportion in each outcome. We calculated the adjusted odds ratio (OR) and 95% confidence intervals (CIs) as an indicator of association between different types of cages and VECF using a logistic regression model. In this model, we introduced a random effect to represent individual differences between surgeons (MS, MU, and others) and adjusted age, sex, treatment level, and surgical techniques (PLIF or TLIF) as potential confounders. Data were statistically analyzed with Stata 15.1 (StataCorp LP, College Station, TX, USA). A value of

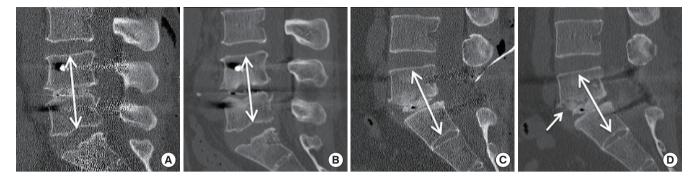


Fig. 1. Methods for radiological assessment using computed tomography (CT) scans taken at day 0 (A, C) and 6-month (B, D) postoperation. Vertebral endplate cyst formation was defined as enlargement of the pre-existing cyst or *de novo* formation of a cyst with a diameter greater than 2 mm (D, arrow) on any section of the multiplanner reconstruction sagittal and coronal images. Cage subsidence was referred as a decrease in the mean distance between the midpoints on the endplates opposite to the side of fusion between day 0 and 6-month postsurgery (A and B, double headed arrow). The distance was measured using the midline section. In the case of L5–S1 fusion, one of the midpoints was used as the upper end of the S1–2 boundary (C and D, double headed arrow).

Table 1. Summary of the 84 patients treated with PLIF/TLIF using the 4 types of cages

Variable	P (n = 20)	Ti (n=16)	TiP (n = 13)	Tn (n = 35)
Age (yr)	66.1 ± 11.2	69.3 ± 11.2	65.8 ± 7.7	68.6 ± 10.8
Female sex	13 (65)	9 (56)	6 (46)	21 (60)
Spinal level				
L3/4 or above	3 (16)	4 (25)	2 (15)	4 (11)
L4/5	15 (75)	10 (63)	11 (85)	26 (74)
L5/S1	2 (10)	2 (13)	0 (0)	5 (14)
Surgeon				
Manabu Sasaki	20 (100)	10 (63)	11 (85)	25 (71)
Masao Umegaki	0 (0)	3 (19)	1 (8)	10 (29)
Others	0 (0)	3 (19)	1 (8)	0 (0)
Surgical technique (TLIF)	6 (30)	1 (6)	1 (8)	3 (9)
Mean pre-VAS-LBP (n = 80) (mm)	43 ± 33	42 ± 25	46 ± 33	43 ± 29
Mean pre-VAS-LP (n=80) (mm)	70 ± 28	68 ± 30	64 ± 32	70 ± 26

Values are presented as mean ± standard deviation or number (%).

PLIF, Posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion; P, polyetheretherketone cage; Ti, titanium cage; TiP, titanium-coating polyetheretherketone cage; Tn, porous tantalum cage; VAS, visual analogue scale; LBP, low back pain; LP, leg pain.

p < 0.05 was considered statistically significant.

RESULTS

1. Preoperative State of the 68 Patients Treated With PLIF/ TLIF Using 4 Types of the Cages

The mean age of patients was 66.1 ± 11.2 years in group P, 69.3 ± 11.2 years in group Ti, 65.8 ± 7.7 years in group TiP, and 68.6 ± 10.8 years in group Tn. The mean preoperative VAS for LBP and LP was 43 ± 33 mm and 70 ± 28 mm in group P,

 42 ± 25 mm and 68 ± 30 mm in group Ti, 46 ± 33 mm and 64 ± 32 mm in group TiP, and 43 ± 29 mm and 70 ± 26 mm in group Tn, respectively. There was no significant difference in patients' mean age, VAS for LBP or VAS for LP between these 4 groups (Table 1).

2. VECF and Types of the Cages

As shown in CT scans of the representative VECF (+) patient in each group (Fig. 2), VECF tended to be multiple and diffuse in groups P and TiP, compared to that in groups Ti and Tn.

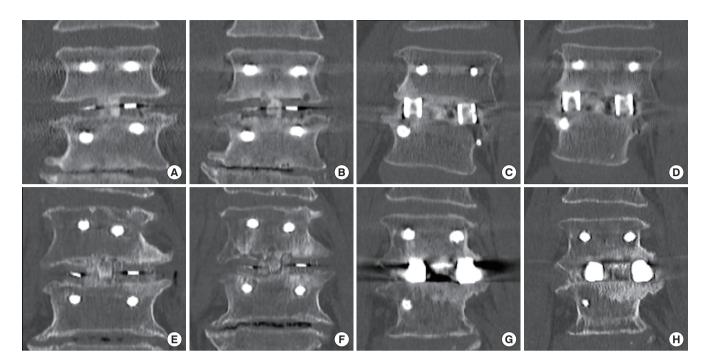


Fig. 2. Computed tomography scans at day 0 (A, C, E, G) and 6-month (B, D, F, H) postoperation showing vertebral endplate cyst formation (VECF) around the polyetheretherketone (PEEK) cages in a 66-year-old man (A, B), the titanium (Ti) cages in a 58-year-old man (C, D), the Ti-coating PEEK cages in a 66-year-old woman (E, F) and the porous tantalum (Tn) cage in a 69-year-old woman (G, H). VECF was multiple and diffused in patients treated with the PEEK cage and the Ti-coating PEEK cage. In contrast, VECF was local and limited in numbers in patients treated with the Ti cage and the porous Tn cage.

Table 2. Radiological and clinical outcomes of the 84 patients

Variable	P(n=20)	Ti (n=16)	TiP (n=13)	Tn (n=35)	p-value
Vertebral endplate cyst formation (+)	13 (65)	7 (44)	9 (69)	8 (23)	0.004
Cage subsidence (+)	10 (50)	5 (31)	8 (62)	5 (14)	0.004
Pain reduction of LBP $(n=80)$	9 (45)	8 (50)	5 (38)	13 (37)	0.850
Pain reduction of LP $(n=80)$	13 (65)	11 (69)	8 (62)	23 (66)	0.990

Values are presented as number (%).

P, polyetheretherketone cage; Ti, titanium cage; TiP, titanium-coating polyetheretherketone cage; Tn, porous tantalum cage; LBP, low back pain; LP, leg pain.

VECF was observed in 13 patients (65%) in group P, 7 patients (44%) in group Ti, 9 patients (69%) in group TiP and 8 patients (23%) in group Tn (Table 2). VECF correlated with types of the cages (p = 0.004) and was the least in group Tn.

A logistic regression analysis showed that the proportion of VECF (+) cases was lower in group Tn than in group P (adjusted OR, 0.16; 95% CI, 0.04–0.60). However, such a difference was not observed in group Ti (adjusted OR, 0.47; 95% CI, 0.10–2.20) or group TiP (adjusted OR, 1.06; 95% CI, 0.21–5.28) when compared to group P (Table 3).

3. Cage Subsidence and Postoperative Pain Reduction

Cage subsidence occurred in 10 patients (50%) in group P, 5 patients (31%) in group Ti, 8 patients (62%) in group TiP, and 5 patients (14%) in group Tn (Table 2). Cage subsidence correlated with the type of cage (p = 0.004), and was the least in group Tn.

Pain reduction in LBP and LP was obtained in 9 (45%) and 13 cases (65%) in group P, 8 (50%) and 11 cases (69%) in group Ti, 5 (38%) and 8 cases (62%) in group TiP, and 13 (37%) and 23 cases (66%) in group Tn, respectively (Table 2). There were no significant differences in the postoperative pain reduction in either LBP or LP (p = 0.85, p = 0.99, respectively).

Type of cage	No. of subjects	Vertebral endplate cyst formation (+), n (%)	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	p-value
P	20	13 (65)	Reference	Reference	
Ti	16	7 (44)	0.42 (0.11-1.61)	0.47 (0.10-2.20)	0.34
TiP	13	9 (69)	1.21 (0.27-5.40)	1.06 (0.21-5.28)	0.94
Tn	35	8 (23)	0.16 (0.05-0.54)	0.16 (0.04-0.60)	0.04

Table 3. Result of a logistic regression analysis for vertebral endplate cyst formation in comparison with group P

P, polyetheretherketone cage; Ti, titanium cage; TiP, titanium-coating polyetheretherketone cage; Tn, porous tantalum cage; OR, odds ratio; CI, confidence interval.

4. Follow-ups After the 6-Month Examination

The mean follow-up period was 62.8 months (range, 19–76 months) in group P, 51.1 months (range, 36–61 months) in group Ti, 35.1 months (range, 16–43 months) in group TiP, and 22.7 months (range, 9–36 months) in group Tn. No patient underwent additional surgery at the fused spinal level during the follow-up periods.

DISCUSSION

The present study suggests that the porous Tn cage has a potential advantage for PLIF/TLIF in the early postoperative period. It is well known that the fusion rate is affected by the type of cage used for lumbar interbody fusion. Previous studies have compared the fusion rate among different types of cages and attempted to find a superior type for arthrodesis. However, the outcomes were not consistent between different studies even when the same type of cage was examined.^{5,6,8} One of the main reasons for such an inconsistency could be a lack of common criteria for the assessment of arthrodesis. CT scans are considered most useful for assessment of the interbody fusion; however, the assessment of union and nonunion is not always consistent among observers. In addition, observation of the interbody space is sometimes difficult due to halation created by metals, such as tantalum, contained in cages. In this study, therefore, instead of arthrodesis we used VECF as our primary outcome. The assessment of VECF is easier than that of arthrodesis and is expected to decrease bias in observers' judgments. Since VECF can develop due to micromotion of the cages between the endplates, presence of VECF suggests that initial stability was not achieved in the cages.

The superiority among different types of interbody cages has been examined from biomechanical and biochemical points of view. As PEEK cage has a higher modulus of elasticity than metal cages, ¹⁰ it is expected to prevent cage subsidence and pseud-

arthrosis by providing a better load transfer to the bone graft. 10,11 However, a few studies have shown that periprosthetic osteolysis and pseudarthrosis occurred more frequently in PEEK cages than in titanium cages. 5,6,11 Some potential causes for the adverse effect associated with PEEK cages have been hypothesized elsewhere. First, the teeth of PEEK cages are not as sharp as those of metal cages due to manufacturing limitations. 12 Therefore, anchoring of the endplates of the PEEK cage is considered weak and insufficient for rigid initial stability. Second, PEEK is not as biocompatible as titanium or tantalum, because of its hydrophobic property.¹¹ A fibrous connective tissue is created at the surface interface of PEEK cage due to inflammatory reaction¹³; in contrast, titanium or tantalum promotes osteogenesis in the adjacent endplates.^{5,14,15} This biochemical reaction in PEEK cages is a disadvantage for early arthrodesis. In order to overcome such a disadvantage, the Ti-coated PEEK cage was introduced. Ti-coating was expected to provide favorable biochemical reactions such as osteogenesis.16

The porous Tn cage resembles a whole trabecular structure with an overall porosity of approximately 80%. Its modulus of elasticity is similar to the cancellous bone that can homogeneously distribute load transfer to the endplate, resulting in minimization of the stress-shielding phenomenon.¹⁷ The surface of the porous structures has a high friction against the endplates, which results in rigid anterior spinal stability.^{18,19} Additionally, the openpore structure facilitates vascularization and osteosynthesis internally.¹⁹ Moreover, tantalum possesses a higher potential for osteoinduction than titanium.^{14,15} These features of the porous Tn cage are considered to be advantageous in providing initial stability and early arthrodesis.

Since April 2013, we started to perform resection of the cartilage endplates and bone grafting as described in this study. We often used the PEEK cage at that time and found that it frequently generated VECF, which had been unremarkable in patients treated with PLIF/TLIF using the Ti cage in our old surgical

^{*}Estimated from logistic regression model adjusted for age, sex, treated level, surgical technique, and surgeon.

method. Thereafter, we used Ti cages, Ti-coated PEEK cages or porous Tn cages, expecting better radiological outcomes. This retrospective study was designed to find a cage that is superior to PEEK. VECF was less in the porous Tn cage than in the PEEK cage. This result suggests that the porous Tn cage could provide rigid initial stability, comparing to the PEEK cage. Additionally, cage subsidence was the least in the porous Tn cage among the cages examined. As full-porous structure can reduce loading stress on the adjacent endplates under any spinal motion,²⁰ the porous Tn cage is expected to reduce cage subsidence.

Contrary to the difference in the radiological outcomes, there was no difference in the clinical outcomes among the 4 types of cages used in this study. Similar results were obtained in the previous studies that showed clinical outcomes did not correlate with periprosthetic osteolysis or pseudoarthrosis.^{2,5,6} It is probable that stabilization with posterior instrumentation eliminates differences in clinical outcomes associated with different types of cages. No patient who had presented severe VECF underwent additional surgery at the fused spinal level during the follow-up periods. Posterior instrumentation might also contribute to this result.

This study has a few limitations. First, this study includes a small number of cases from a single facility. Although the logistic regression analysis shows that Tn cage significantly reduces VECF comparing to PEEK cage, the power of statistical analysis might be insufficient to demonstrate superiority among the other cages. Second, although we adjusted for many potential confounders, the outcomes could still be affected by unmeasured confounders, such as bone quality. In Japan, bone mineral density measurement is permitted in the aged patients or the younger ones with certain disease affecting bone quality. As such, we cannot extrapolate a definitive outcome from this observational study because of these limitations. However, we believe that the preliminary result of this study will be helpful for cage selection despite these limitations.

CONCLUSION

The present study showed that VECF was least detected in the porous Tn cage among all cases that we examined. This result suggests that Tn cages could produce rigid initial spinal stability. This advantage is probably attributed to its material property and unique structure. Thus, it is a favorable option in patients undergoing PLIF/TLIF procedures.

CONFLICT OF INTEREST

The authors have nothing to disclose.

ACKNOWLEDGMENTS

Part of the data in this manuscript was presented in the 10th annual meeting of ASIA SPINE 2019.

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