Comparison of Short-Term Radiographical and Clinical Outcomes After Posterior Lumbar Interbody Fusion With a 3D Porous Titanium Alloy Cage and a Titanium-Coated PEEK Cage

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Abstract

Study Design: Clinical case series.

Objectives: To compare the short-term (≤ 1 year) radiographical and clinical outcomes between posterior lumbar interbody fusion (PLIF) with a titanium-coated poly-ether-ether-ketone (TCP) cage and PLIF with a three-dimensional porous titanium alloy (PTA) cage.

Methods: Overall, 63 patients who had undergone 1- or 2-level PLIF since March 2015 were enrolled (median age, 71 years). The first 34 patients underwent PLIF with TCP cages (until June 2017) and the next 29 patients with PTA cages. Fusion status, vertebral endplate cyst formation (cyst sign: grade 0, none; grade 1, focal; and grade 2, diffuse), cage subsidence (grade 0, < 1 mm; grade 1, 1–3 mm; and grade 2, > 3 mm), and patient-reported quality of life (QOL) outcomes based on the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ) were compared at 6 months and 1 year postoperatively between the 2 cage groups.

Results: Cyst sign and cage subsidence grades were significantly lower in the PTA cage group than in the TCP cage group at 6 months postoperatively (cyst sign, p = 0.044; cage subsidence, p = 0.043). In contrast, the fusion rate and surgery effectiveness based on JOABPEQ at both 6 months and 1 year postoperatively were not different between the 2 groups.

Conclusions: Patient-reported QOL outcomes were similar between the TCP and PTA cage groups until 1 year postoperatively. However, a higher incidence and severity of postoperative vertebral endplate cyst formation in patients with the TCP cage was a noteworthy radiographical finding.

Keywords
titanium-coated poly-ether-ether-ketone, three-dimensional porous titanium, cage, vertebral endplate cyst, subsidence, quality of life

Introduction

Since the first experimental use of titanium (Ti) or carbon poly-ether-ether-ketone (PEEK) cages for lumbar interbody fusion in humans in the 1990s,1 various interbody fusion cages have been used to promote fusion and maintain spinal alignment in lumbar interbody fusion surgeries. Given that Ti and PEEK are biocompatible, they remain the most common materials for interbody fusion cages. PEEK interbody fusion cages have been more widely used because the radiolucency of PEEK is

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favorable for assessing radiographical fusion status, and the elastic modulus of PEEK, equivalent to that of the bone, is considered advantageous for preventing cage subsidence and promoting bone union.2,3

However, the chemical inertness and hydrophobic nature of PEEK, which confer biocompatibility, limit direct cell adhesion on PEEK implant surfaces, and fibrous tissue surrounding the implant surfaces has been observed after the implantation of PEEK implants in the bone in animal studies.4,6 Furthermore, compared with Ti surface, suppression of osteoblastic differentiation of mesenchymal stem cells and activation of inflammatory responses have been observed on PEEK surface in vitro.7,8 Clinically, Nemoto et al.9 reported poorer radiographical outcomes owing to pseudoarthrosis after lumbar interbody fusion with PEEK cages than with Ti cages. Therefore, Ti has garnered increasing attention as an interbody fusion cage material because of its superiority over PEEK regarding bioactivity on the bone.10

The disadvantage of Ti is its higher stiffness than that of bone, which can cause stress shielding on the grafted bone and cage subsidence.2,11,12 Recent development of biomaterial processing technologies has helped provide interbody fusion cages with an elastic modulus equivalent to that of bone along with the osteoconductivity of Ti on the frame surfaces. One such cage is made of Ti-coated PEEK (TCP) and another is made of three-dimensional (3D) porous Ti alloy (PTA). These have been developed to improve short-term outcomes after spinal interbody fusion surgeries by promoting initial fixation on the cage surfaces, and favorable radiographical, histological, and clinical outcomes have been reported.4,6,13-17 Nevertheless, the differences in the radiographical and clinical outcomes between TCP and PTA cages remain unclear. Conceptually, the micro-interconnected porous structure of the PTA cage frames can permit deep ingrowth of stem cells or osteoblasts into the cage frames. In TCP cages, the ingrowth can occur only on the Ti-coated layer above PEEK frames. Thus, we hypothesized that PTA cages will provide better outcomes because of their potential for deeper bone ingrowth into the cage frames compared with TCP cages.

The study aim was to identify the differences between and relative merits of 1-year postoperative radiographical and patient-reported quality of life (QOL) outcomes after posterior lumbar interbody fusion (PLIF) between TCP and PTA cages.

Methods
This retrospective review of prospectively collected data was approved by the research ethics committee of our institution. The research protocol was approved and publicized by our institution. The research ethics committee of our institution waived the written informed consent to be obtained from the patient because all clinical and radiographic interventions in this study followed routine assessment and this study was retrospective study design. Instead, the patients were given the right to opt out of the study based on the research information published on the website of our institution.

Patients and Surgical Procedure
All consecutive patients (n = 73) who had undergone 1- or 2-level PLIF (including those undergoing concomitant laminectomies at other levels) for degenerative lumbar disorders since March 2015 were enrolled. The indications of PLIF were spondylolisthesis with slippage >3 mm and/or a posterior opening >5° on dynamic lateral plain radiographs and/or foraminal stenosis requiring total facetectomy for decompression. Four patients with previous spinal fusion surgeries, additional spinal surgeries after PLIF, hemodialysis owing to renal failure, and/or scoliosis (Cobb angle > 30°) were excluded. Six patients failed to complete postoperative follow-up (TCP cage group, 5 patients; PTA cage group, 1 patient). Thus, finally, 63 patients (25 men and 38 women) were included in this study. The median age at the time of surgery of all patients was 71 (interquartile range [IQR], 64–76) years. PLIF was performed using the conventional open method with bilateral total facetectomy using cages, pedicle screws, and rods. After removing the disc material and preparing the vertebral endplates taking care not to break the endplates, 2 cages were inserted in each intervertebral space. Local autologous bone was used as bone graft material in the cages and intervertebral space in all cases, without bone morphogenetic protein or allograft bone. Partial laminectomy was performed in cases with concomitant canal stenosis at other levels. The TCP cages (ProSpace XP; Aesculap AG, Tuttingen, Germany; pore size, 50–200 μm; mean porosity, 37.3%; elastic modulus, 4.6 GPa) were used until June 2017 (34 patients) and the PTA cages (Tritanium PL; Stryker, Kalamazoo, MI; Tritanium PL; Stryker, Kalamazoo, MI; pore size, 100–700 μm; mean porosity, 60%; elastic modulus, 6.2 GPa) after July 2017 (29 patients).

Patients’ Demographic and Operative Data
Age at the time of surgery, sex, pathologies for spinal surgery, body mass index, diabetes mellitus history, estimated glomerular filtration rate, PLIF segment level, total number of decompression segments, and preoperative T-score of the lumbar spine (L2–L4) and proximal femur calculated using dual-energy x-ray absorptiometry (Horizon; Hologic, Inc., Marlborough, MA) were obtained from medical charts and operative notes.

Radiographical Assessments
Spinal alignment. The following parameters were measured on preoperative plain standing lateral radiographs taken in the neutral position: pelvic incidence (PI), lumbar lordosis (LL: L1–S1; +, lordosis), and pelvic tilt (PT). The preoperative differences between PI and LL (PI – LL) were calculated, and age-specific ideal PT and PI – LL were generated according to previously published formulæ18:

\[
\text{Ideal PT} = \frac{(\text{Age} - 55)}{3} + 20
\]

\[
\text{Ideal PI} - \text{LL} = \frac{(\text{Age} - 55)}{2} + 3
\]
The preoperative differences between actual PT and ideal PT (offset PT: actual PT – ideal PT) and between actual PI – LL and ideal PI – LL (offset PI – LL: actual [PI – LL] – ideal [PI – LL]) were calculated.

Fusion angle (FA: the angle between the superior endplate of the upper instrumented vertebra and the inferior endplate of the lower instrumented vertebra [LIV] or superior endplate of S1 in cases where LIVs were S1; +, lordosis) was measured on preoperative and 1-year postoperative plain standing lateral radiographs taken in the neutral position, and the perioperative changes in values ([1-year postoperative values] – [preoperative values]) of FA were also calculated.

Hounsfield unit (HU) values of instrumented vertebrae on computed tomography (CT) images. CT was performed using either of 2 scanners (Discovery CT750 HD; GE Healthcare Japan, Tokyo, Japan or Aquilion ONE; CANON MEDICAL SYSTEMS CORPORATION, Tochigi, Japan) preoperatively, and at 6 months and 1 year postoperatively. CT has been performed routinely at our institution for preoperative planning and postoperative evaluation of bony fusion or instrumentation failure, both of which are difficult to clearly detect using magnetic resonance imaging. The settings used were as follows: slice thickness, 0.625 mm on the Discovery CT750 HD and 0.5 mm on the Aquilion ONE; tube voltage, 120 kVp; matrix, 512 × 512; and algorithm, standard. The tube current was maintained by an automatic exposure control system to reduce radiation exposure dose. Image processing was performed at our institution using a built-in 3D imaging software (Synapsee Vincent; Fujifilm Holdings Corporation, Tokyo, Japan). HU values of instrumented vertebrae were measured from preoperative CT images to assess bone mineral density using Schreiber’s method.\(^{19}\) The mean HU values of all instrumented vertebrae in each patient were calculated.

**Fusion assessment of PLIF segments using CT images and dynamic lateral plain radiographs.** Fusion status was evaluated at the 6-month and 1-year postoperative follow-ups on the basis of modifications described in previously reported methods.\(^{20,21}\) Briefly, fusion was defined when both of the following criteria were fulfilled: (1) formation of a bone bridge between the upper and lower vertebral bodies or a thick fusion mass with no translucency around the cages on CT images and (2) a flexion–extension angle ≤ 5° with no translucency around the cages on dynamic lateral plain radiographs.

**Vertebral endplate cyst formation and cage subsidence on CT images.** Vertebral endplate cyst formation (cyst sign) and cage subsidence were evaluated on 6-month and 1-year postoperative CT images at each PLIF segment. A positive cyst sign was defined according to a previous report,\(^{22}\) and the cyst sign was graded as follows: grade 0, no positive cyst sign; grade 1, focal positive cyst sign appearing only around the corners of the cages; and grade 2, diffuse positive cyst sign with multiple and widespread emergence. Cage subsidence was graded according to a previous report: grade 0, < 1 mm; grade 1, 1–3 mm; and grade 2, > 3 mm.\(^{23}\) The highest cyst and subsidence grades of each PLIF segment were adopted.

**Evaluation of Patient-reported QOL Outcomes**

Patient-reported QOL was evaluated according to the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ). The 5 categories in JOABPEQ (pain-related disorders, lumbar spine dysfunction, gait disturbance, social life function, and psychological disorders), both preoperatively and at the 1-year postoperative follow-up time point, were calculated for each patient. According to the JOABPEQ user guide,\(^{24}\) after excluding patients with both pre- and postoperative scores ≥ 90 points, the surgery was judged as effective or not for individual patients in each category. The effectiveness rate of surgery was calculated in each category according to the following formula: (number of patients whose surgeries were judged “effective”) / ([total number of patients] – [number of patients with both pre- and postoperative scores ≥ 90 points]) × 100 (%).\(^{24}\)

**Statistical Analysis**

Statistical analysis was performed using IBM SPSS Statistics Version 25 (IBM, Armonk, NY, USA). Mann–Whitney U test was performed to compare continuous variables and Fisher’s exact probability test to compare categorical variables between the TCP and PTA cage groups. Significance level was set at \(p < 0.05\).

**Results**

Patients’ demographic and operative data in each cage group is shown in Table 1. The median total number of decompression segments was significantly larger in the PTA cage group (2 [IQR, 1–2]) than in the TCP cage group (1 [IQR, 1–2]) \((p = 0.016)\). The median T-score of the lumbar spine was significantly higher in the PTA cage group than in the TCP cage group \((p = 0.002)\) although preoperative HU values of instrumented vertebrae were not different between the groups (Table 1). Preoperative spinal alignment and perioperative changes in FA values were not different between the groups (Table 2). Offset of PT and PI – LL did not differ between the groups preoperatively (Table 2).

PLIF was performed at 39 and 36 intervertebral segments in the TCP and PTA cage groups, respectively. The fusion rates were not different between the groups at 6 months and 1 year postoperatively (Table 3).

**Vertebral Endplate Cyst Formation (Cyst Sign)**

In the TCP cage group, grade 0 was observed in 7, grade 1 in 20, and grade 2 in 12 segments 6 months postoperatively (Figure 1). In the PTA cage group, grade 0 was observed in 16, grade 1 in 12, and grade 2 in 8 segments 6 months postoperatively (Figure 1). The median 6-month postoperative cyst sign...
grade was significantly higher in the TCP cage group (1 [IQR, 1–2]) than in the PTA cage group (1 [IQR, 0–1]) (p = 0.044).

**Cage Subsidence**

In the TCP cage group, grade 0 was observed in 24, grade 1 in 11, and grade 2 in 4 segments 6 months postoperatively (Figure 2), and grade 0 was observed in 23, grade 1 in 9, and grade 2 in 7 segments 1 year postoperatively (Figure 3). In the PTA cage group, grade 0 was observed in 30, grade 1 in 4, and grade 2 in 2 segments 6 months postoperatively (Figure 2), and grade 0 was observed in 23, grade 1 in 9, and grade 2 in 4 segments 1 year postoperatively (Figure 3). The median 6-month postoperative cage subsidence grade was significantly higher in the TCP cage group (0 [IQR, 0–1]) than in the PTA cage group (0 [IQR, 0–0]) (p = 0.043); however, the median 1-year postoperative cage subsidence grade was not different between the TCP (0 [IQR, 0–1]) and PTA (0 [IQR, 0–1]) cage groups (p = 0.557).

**Patient-Reported QOL Outcomes (JOABPEQ)**

The median preoperative scores in the pain-related disorders and social life function categories of the JOABPEQ were significantly higher in the TCP cage group than in the PTA cage group (p = 0.014; Table 4). Preoperative scores in the other JOABPEQ categories were not different between the 2 groups (Table 4). The postoperative effectiveness rates in all the JOABPEQ categories were equivalent between the 2 groups at both 6 months and 1 year postoperatively (Table 5).

**Discussion**

This study showed that the median 6-month postoperative cyst sign and cage subsidence grades were higher in the TCP cage group than in the PTA cage group. However, 1 year after PLIF, the cage subsidence grades were not different between the groups. The fusion rate and effectiveness rate of PLIF in all
QOL categories based on the JOABPEQ were comparable between the TCP and PTA cage groups at both 6 months and 1 year postoperatively. To the best of our knowledge, this is the first study to report differences in the radiographical and clinical outcomes after PLIF between TCP and PTA cages.

Currently, among aging societies, the number of elderly individuals that undergo lumbar arthrodesis for various degenerative diseases has been increasing. PLIF and posterolateral fusion (PLF) are the most commonly performed surgical procedures for lumbar arthrodesis. Several authors reported that there was no significant difference between PLIF and PLF in terms of clinical outcome, complication rate, operative time, and blood loss. However, a recent review showed that PLIF is advantageous over PLF in terms of higher fusion rate and better restoration of lumbar alignment. Therefore, PLIF has been the first choice for lumbar arthrodesis treatment in our institution, regardless of the age of the patients. In this study, the median age at the time of surgery was >70 years. In elderly individuals, instrumentation failure, such as cage subsidence and screw loosening, and delayed or nonunion because of poor bone strength or low osteogenic quality of autologous bone graft due to osteoporosis are great concerns after PLIF.
Biological approaches to enhance bone quality and strength, including pharmacological, cell, and gene therapies, have been used,30 and various improvements in implant materials and shapes have also been made. One such attempt at improvement was the development of TCP and PTA cages to utilize the biocompatibility (osteocompatibility) of Ti. Osseointegration of Ti or Ti alloy is a favorable property for intervertebral cages because direct bonding between bone and implant surfaces can promote initial fixation of the cages. This cannot be well observed on the surfaces of pure-PEEK materials because they are often observed to be surrounded by relatively dense fibrous tissue after implantation into bone.4-6

A recent review comparing the radiographical and clinical outcomes between PEEK and TCP cages concluded that fusion rate and clinical outcomes were similar after lumbar or cervical interbody fusion surgeries.31 A randomized controlled trial by Rickert et al.16 also showed that transforaminal lumbar interbody fusion with a TCP cage could achieve favorable radiographical and clinical outcomes compared to that with a PEEK cage with the same geometry. However, to date, it remains unclear whether TCP or PTA cage provides better radiographical and clinical outcomes after lumbar interbody fusion surgery.

Radiographically, the ability to maintain postoperative local and spinopelvic alignments was similar between the TCP and PTA cages in this study; however, compared with the former,
the latter significantly restrained early (6-month) postoperative vertebral endplate cyst formation and progression and cage subsidence. Vertebral endplate cysts are reportedly good predictors of nonunion or delayed union after lumbar interbody fusion and are thought to appear in the presence of micromotion in the fused segments where stress-induced microfracture and bone resorption can occur.\textsuperscript{22,32} The relationship between subchondral bone cyst formation and mechanical stress in osteoarthrosis was demonstrated in a finite element analysis,\textsuperscript{33} and we speculated that the mechanical stress due to micromotion at the corners of the cages could cause local bone resorption (cyst sign, grade 1). Under such conditions, cage subsidence is also likely to occur. Therefore, this suppressive effect of PTA cage is attributable to its better initial fixation and ability to achieve deeper bone ingrowth into the cage frames than TCP cage. Another concern is Ti coating delamination at the time of TCP cage insertion, which is a drawback of these cages.\textsuperscript{34,35} We suppose that this delamination occurs not only at the impaction of TCP cages but also under the continuous micromotion in nonfusion segments after PLIF in osteoporotic patients. The wear particles from the Ti coating allow phagocytosis or inflammation reaction on the implant surface,\textsuperscript{36,37} leading to vertebral endplate cyst formation and diffuse spread of the cysts on the vertebral endplates (cyst sign, grade 2) (Figure 4).

Fusion status has a significant effect on the postoperative QOL outcomes after lumbar arthrodesis.\textsuperscript{38} In this study, the fusion rates were not different between the 2 groups postoperatively at 6 months and 1 year. Thus, the similarities in postoperative QOL outcomes for every JOABPEQ category between the TCP and PTA cage groups could have resulted from similar postoperative fusion rates between these groups at 6 months and 1 year postoperatively. In our patients, not only intervertebral cages but also autologous bone was transplanted into the intervertebral spaces during PLIF. Even if bone ongrowth on the cage frame surfaces was insufficient, the transplanted autologous bone could help achieve fusion and similar radiographical outcomes 1 year postoperatively. We believe that autologous bone transplant is essential even when using TCP or PTA cage to achieve fusion and better clinical outcomes.

There are several limitations of our study. First, the geometry and elastic modulus of the TCP and PTA cages were not identical. The differences in the microstructure of the cage surface and teeth shape or frame thickness between the cages can affect vertebral endplate cyst formation and cage subsidence. Second, the follow-up period was short. Because the TCP and PTA cages were developed mainly for promoting early postoperative initial fixation between the cage surface and vertebral endplates, we focused on the differences in early postoperative radiographical and clinical outcomes between these cages. Thus, long-term outcomes and adverse effects of these cages remain unknown. Third, this study has an intrinsic historical bias without randomization. Further randomized controlled studies with long-term follow-up are desirable to confirm the clinical superiority of TCP and PTA cages.

In conclusion, we compared 1-year postoperative radiographical and clinical outcomes of PLIF with TCP cage with those of PLIF with PTA cage. Our results showed that the maintenance of spinal alignment, severity of 1-year postoperative

**Figure 4.** A typical example of a vertebral endplate cyst formation in the titanium-coated poly-ether-ether-ketone (TCP) cage group (A 75-year-old male patient with L3/L4/L5 posterior lumbar interbody fusion: left, 1 week postoperatively; right, 6 months postoperatively). Diffuse vertebral endplate cysts (arrow heads, cyst sign, grade 2) and a huge cyst with marginal sclerosis (arrows) were observed on the adjacent vertebral endplates on the surface of the TCP cage at L4/L5 (nonunion segment), while no cyst could be found at L3/L4 (union segment).
cage subsidence, and fusion rate and patient-reported QOL outcomes at 6 months and 1 year postoperatively were similar between the 2 groups. In contrast, the incidence and severity of 6-month postoperative vertebral endplate cyst formation and cage subsidence were less in the PTA cage group than in the TCP cage group, with diffuse spread of vertebral endplate cyst at 6 months postoperatively being a noteworthy early postoperative radiographical finding in the latter. These facts suggest that PTA cage is superior over TCP cage regarding early postoperative initial fixation strength, which is the main purpose of these cages.

**Authors’ Note**

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**Declaration of Conflicting Interests**

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: TM reports personal consulting fee from Stryker Japan outside the submitted work. TK reports personal consulting fee from Medacta, Kyocera, and Nuvasive outside the submitted work, and receives research grant from B/Braun Aesculap outside the submitted work. TK reports personal consulting fee from Medacta, Kyocera, and Nuvasive outside the submitted work, and receives research grant from B/Braun Aesculap outside the submitted work.

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