SPANDIDOS PUBLICATIONS

EXPERIMENTAL AND THERAPEUTIC MEDICINE 25: 305, 2023

Titanium-coated polyetheretherketone cages vs. polyetheretherketone cages in lumbar interbody fusion: A systematic review and meta-analysis

SONGFENG LI[1,2*], XIYONG LI[1,2*], XIAOHUI BAI[1,2], YUNLU WANG[1,2], PENGFEI HAN[1] and HONGZHUO LI[1]

[1]Department of Orthopaedics, Heping Hospital Affiliated to Changzhi Medical College;
[2]Graduate School, Graduate Student Department of Changzhi Medical College, Changzhi, Shanxi 046000, P.R. China

Received November 4, 2022; Accepted April 14, 2023

DOI: 10.3892/etm.2023.12004

Abstract. Fusion material is one of the key factors in the success of lumbar interbody fusion surgery. The present meta-analysis compared the safety and efficacy of titanium-coated (Ti) polyetheretherketone (PEEK) and PEEK cages. Published literature on the use of Ti-PEEK and PEEK cages in lumbar interbody fusion was systematically searched on Embase, PubMed, Central, Cochrane Library, China National Knowledge Infrastructure and Wanfang databases. A total of 84 studies were retrieved and seven were included in the present meta-analysis. Literature quality was assessed using the Cochrane systematic review methodology. After data extraction, meta-analysis was performed using the ReviewManager 5.4 software. Meta-analysis showed that, compared with that in the PEEK cage group, the Ti-PEEK cage group showed a higher interbody fusion rate at 6 months postoperatively (95% CI, 1.09-5.60; P=0.03) and improved Oswestry Disability Index (ODI) scores at 3 months postoperatively [95% CI, -7.80-(-0.62); P=0.02] and visual analog scale (VAS) scores of back pain at 6 months postoperatively [95% CI, -0.8-(-0.23); P=0.0008]. However, there were no significant differences in intervertebral bone fusion rate (12 months after surgery), cage subsidence rate, ODI score (6 and 12 months after surgery) or VAS score (3 and 12 months after surgery) between the two groups. The results of the meta-analysis showed that the Ti-PEEK group had an improved interbody fusion rate and higher postoperative ODI score in the early postoperative period (≤6 months).

Correspondence to: Professor Pengfei Han or Professor Hongzhuo Li, Department of Orthopaedics, Heping Hospital Affiliated to Changzhi Medical College, 110 South Yan'an Road, Changzhi, Shanxi 046000, P.R. China
E-mail: 18003551149@163.com
E-mail: lihz0999@sina.com

*Contributed equally

Key words: titanium-coated polyetheretherketone, lumbar interbody fusion, meta-analysis

Introduction

Lumbar interbody fusion (LIF) is used to treat pathological spinal changes caused by lumbar degenerative disease, trauma, infections, congenital malformations, tumors and other diseases (1). LIF is one of the most common types of spinal surgery used to provide support between the vertebral bodies to stabilize the vertebral structure, restore lordosis, correct deformity and provide indirect decompression of compressed nerves, which is shown to have good clinical effects in the treatment of spinal disease (2). Technological developments have gradually evolved into a variety of intervertebral space treatment methods and implant materials. Interbody fusions include anterior, direct lateral, oblique lateral and transforaminal. The types of implants used in fusion also vary. The most commonly used materials for fusion grafts are Ti, PEEK and newer generation implants (3). The material of the interbody fusion cage is a key factor in interbody fusion. An ideal fusion material must be sufficiently rigid to maintain stability and have an elastic modulus similar to that of bone to prevent subsidence and stress shielding (4). Titanium (Ti) has been used in orthopedic surgery since the 1940s owing to its excellent biocompatibility, low toxicity and good mechanical properties (5). However, Ti has poor radiation penetration and a large elastic modulus (70-100 GPa), which is higher than the 18.6 GPa of the cortical bone and can easily lead to complications such as the sinking of the lumbar interbody fusion apparatus (6). With the development of medical-grade polyetheretherketone (PEEK), PEEK has been used as a potential replacement material for Ti cages in lumbar interbody fusion since the 1990s. Several studies showed that the PEEK elastic modulus is close to that of human cortical bone (7), which gives PEEK cages advantages in spine load distribution and stress distribution (8). PEEK was shown to have excellent radiation penetration and could be used to evaluate the progress of intervertebral bone fusion using X-rays (9). According to Setzer *et al* (10), PEEK fusion devices are the most commonly used because of their excellent elastic modulus and effective fixation. However, PEEK also has a few hydrophilic groups

that do not provide sufficient space for cell adhesion (11). The biological inertness of the material is related to its inability to integrate well with the surrounding bone (12) and its non-bone conductivity characteristics adversely affect bone fusion (3,9). One of the techniques currently used to improve the biological function of existing implants is to treat cage surfaces with osteoconductive materials to increase fusion rate and improve integration of the implant (3,9). With the development of low-temperature coating technologies, Ti metal has been combined with PEEK. Ti is coated on a PEEK surface using a low-temperature coating process to enhance the biocompatibility of the PEEK surface in a new type of interbody fusion device, the Ti-PEEK cage, with the advantages of both materials (7,13). Han *et al* (13) found through *in vivo* and *in vitro* experiments that the biocompatibility of PEEK was significantly improved after Ti coating and the wettability, cell reactivity and bone conductivity of the PEEK cage also improved, indicating that the Ti-PEEK cage had high application potential in vertebral fusion surgery. Therefore, the present study aimed to compare these differences using a meta-analysis to provide theoretical guidance for clinical practice.

Materials and methods

Included data. The subjects were those included in published controlled clinical studies. Non-case-control studies, case reports, literature reviews, letters and repeated reports were excluded. Literature that included cases which did not provide enough relevant data was also excluded. Based on the patient medical history, physical examination and imaging examination, all patients underwent lumbar fusion. The intervention measures were Ti-PEEK and PEEK cages. The outcome indicators were bone fusion rate, cage settlement rate, postoperative Oswestry Disability Index (ODI) score and postoperative lower back pain visual analog scale (VAS) score (14-20).

Search strategy. A comprehensive search of the Embase (embase.com), PubMed (pubmed.ncbi.nlm.nih.gov/), Central Cochrane Library (https://www.cochranelibrary.com/), China National Knowledge Infrastructure (https://www.cnki.net/) and Wanfang databases (https://www.wanfangdata.com.cn/) was performed. Additionally, a manual search of journal catalogues and bibliographical references was performed to find grey literature, such as unpublished academic papers and chapters in monographs. All relevant documents were searched in any language and translated if necessary. No language restrictions were imposed. The English search terms were 'titanium-coated polyetheretherketone', 'Ti-PEEK', 'polyetheretherketone', 'PEEK', 'lumbar interbody fusion' and 'LIF'.

Quality assessment of the literature. The included studies were independently analyzed by two authors and disagreements were resolved through discussion or handed over to a third author to determine the quality of the literature. This was done in strict accordance with the Cochrane risk of bias assessment criteria (21) as follows: i) Experimental design adopts randomization; ii) double blinding; iii) experimental data is complete and reliable; iv) allocation concealment is used; v) selective data reporting method; or vi) other bias. The quality of the literature was also evaluated according to the Newcastle-Ottawa scale (NOS) (22), with a total score of nine points as follows: The representativeness of the exposed group (true or representative of the community population), 1 point; choice of the non-exposed cohort (from the same community as an exposed cohort), 1 point; determination of exposure factors (reliable records or structured surveys), 1 point; no outcome to observe at the start of the study (yes), 1 point; comparability between groups, ≤2 points; double-blind principle, 1 point; follow-up time length (≥2 years), 1 point and no loss to follow-up (loss rate <15%), 1 point. A total score of ≥7 was considered high-quality case study literature.

Statistical analysis. ReviewManager 5.4 software (training.cochrane.org/online-learning/core-software/revman) was used to analyze the extracted data. Secondary variables are expressed using Q-test, odds ratios (ORs) and 95% CIs. Continuous variables are represented as mean or standardized mean differences and 95% CIs. The I^2 value was calculated to test the heterogeneity between studies. When $I^2<50\%$, the heterogeneity between the studies was considered small and a fixed-effects model was used. If $I^2>50\%$, the heterogeneity between studies was considered large and the cause of heterogeneity was analyzed using a random-effects model. A sensitivity analysis was conducted by removing some studies and creating funnel charts to evaluate publication bias. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Search results. Using the aforementioned strategy, 84 relevant studies were retrieved. After reading the titles and abstracts, 53 non-controlled studies, repeated publications and articles irrelevant to the research purpose were excluded and 31 relevant articles were screened. After reading the full text, the inclusion and exclusion criteria were strictly followed for screening and yielded seven studies (14-20). All the included studies compared the baseline conditions of the patients, such as age and disease duration, which were comparable ($P>0.05$). A flowchart of the literature search strategy is shown in Fig. 1; basic characteristics of the included literature are shown in Table I.

Quality evaluation of the included studies. The present study included four randomized controlled trials, two prospective studies and one retrospective study. NOS was used for quality evaluation. One trial scored 9 points, four trials scored 8 points, and two trials scored 7 points, equaling a total of seven high-quality and zero low-quality articles. The methodological evaluation of the included studies was performed using Cochrane Tools of Risk of Bias (training.cochrane.org/online-learning/core-software/revman) and the evaluation items included random assignment method, hidden grouping, blinding of participants, blinding of analysts, completeness of outcome data, selective reporting of study results and other sources of bias. For each entry, a judgment of low risk, unclear or high risk was made. The risk of bias is shown in Fig. S1. Although the number of included studies was limited and there was some bias, the overall quality was moderate.

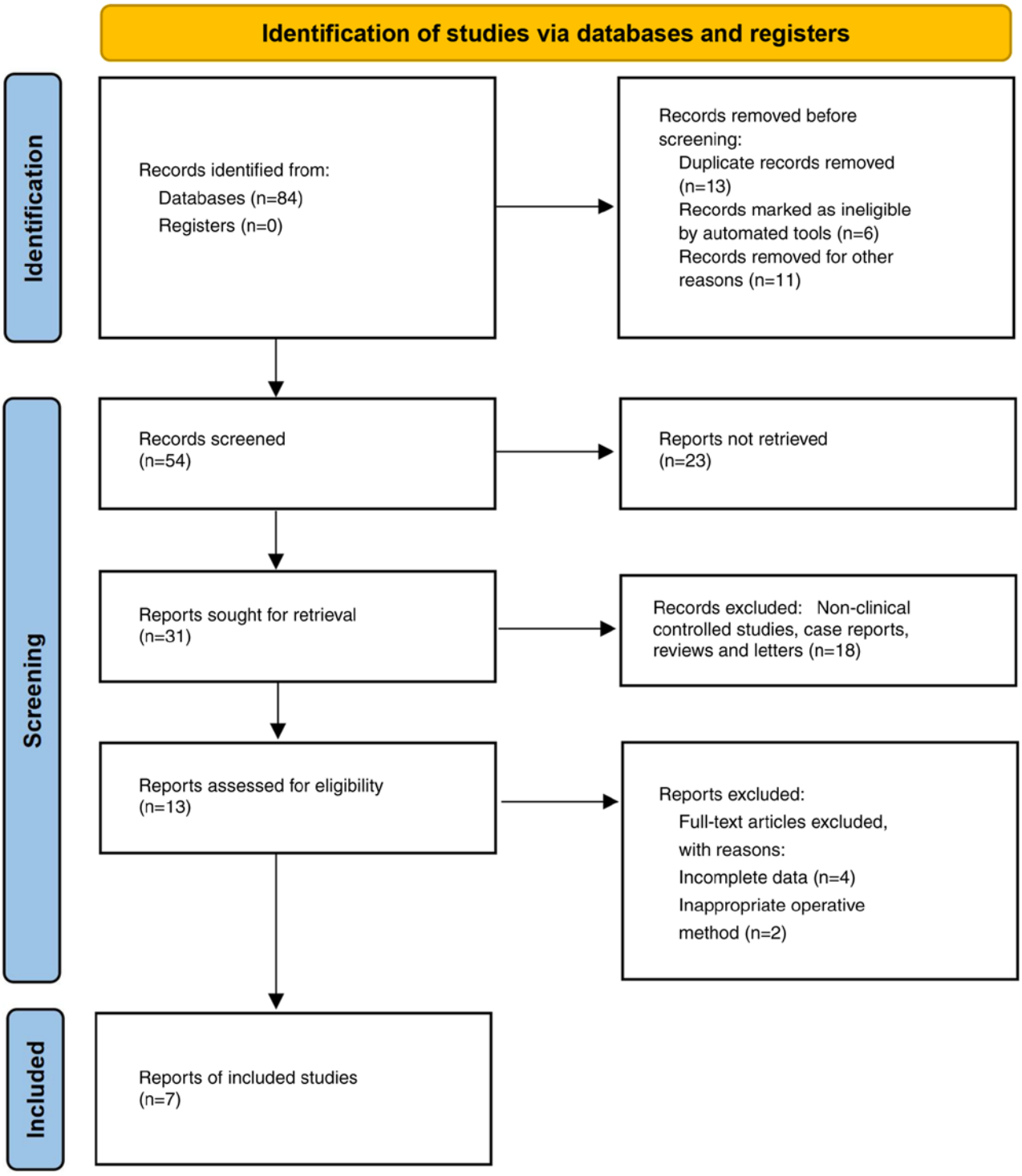

Figure 1. Flow diagram of study identification and selection.

Meta-analysis results

Comparison of postoperative bone fusion rates. A total of five studies reported the postoperative bone fusion rates at 6 months after surgery comparing Ti-PEEK and PEEK (429 patients, 208 in the Ti-PEEK group and 221 in the PEEK group). Heterogeneity tests showed heterogeneity between the five studies (I^2=65%; Q-test, P=0.02; Fig. 2). Effect sizes were combined using the random-effects model and showed statistical significance (Z=2.18; P=0.03; OR, 2.48; 95% CI, 1.09-5.60), suggesting that the Ti-PEEK group had a superior lumbar interbody fusion rate compared with that in the PEEK group 6 months postoperatively. A total of six studies reported postoperative bone fusion rates (12 months) comparing Ti-PEEK and PEEK (492 patients, 236 in the Ti-PEEK group and 256 in the PEEK group). Heterogeneity tests were performed on the six studies and the results showed no heterogeneity (I^2=43%; Q-test, P=0.12) and the fixed-effects model was used to combine effect sizes. The results of the meta-analysis showed no statistically significant difference between the two groups (Z=0.60;

Table I. Baseline characteristics of the studies included in the meta-analysis.

First author/s, year	Study design	Country	Groups	Patients, n	Mean age, years	Sex, male/female	Outcomes	Newcastle-Ottawa scale	(Refs.)
Hasegawa *et al*, 2020	Prospective	Japan	Ti-PEEK	69	67.4±10.9	38/31	(1) (2) (3)	7	(14)
			PEEK	80	67.0±10.6	46/34			
Rickert *et al*, 2017	RCT	Germany	Ti-PEEK	20	67.7±12.5	6/14	(1) (2) (3) (4)	8	(15)
			PEEK	20	68.3±10.5	6/14			
Sakaura *et al*, 2021	Prospective	Japan	Ti-PEEK	32	70.8±11.2	13/19	(1)	7	(16)
			PEEK	37	69.3±10.0	19/18			
Schnake *et al*, 2021	RCT	Germany	Ti-PEEK	28	52.9±32.7	13/15	(1) (2) (3) (4)	9	(17)
			PEEK	27	50.6±33.3	6/21			
Singhatanadgige *et al*, 2022	RCT	Thailand	Ti-PEEK	41	62.73±9.5	15/26	(1) (2)	8	(18)
			PEEK	41	64.12±11.5	13/28			
Willems *et al*, 2019	RCT	Belgium	Ti-PEEK	44	50.0±9.7	17/27	(1) (3) (4)	8	(19)
			PEEK	37	51.5±8.4	21/16			
Yao *et al*, 2023	Retrospective	China	Ti-PEEK	27	67.9±13.4	6/21	(1) (2) (3) (4)	8	(20)
			PEEK	27	68.6±10.3	6/21			

RCT, randomized controlled trial; Ti-PEEK, titanium-coated polyetheretherketone; (1), bone fusion rate; (2), cage subsidence rate; (3), postoperative Oswestry Disability Index score; (4), visual analog scale of back pain.

P=0.55; OR, 1.22; 95% CI, 0.64-2.33), suggesting that the Ti-PEEK and PEEK groups had similar rates of lumbar interbody fusion at 12 months postoperatively. Combined with the aforementioned results, this suggested the Ti-PEEK group exhibited increased osteocyte growth compared with that of the PEEK group, which in turn increased the rate of intervertebral fusion in the short term (<6 months); however, the rate of vertebral fusion was the same between the two groups in the long term (>12 months; Fig. 2).

Comparison of postoperative cage subsidence rates (6-12 months after surgery). A total of five studies reported postoperative cage subsidence rates comparing the Ti-PEEK and PEEK groups (394 patients, 191 in the Ti-PEEK group and 203 in the PEEK group). As the heterogeneity test showed no statistically significant heterogeneity between the five studies (I^2=0%; Q-test, P=0.74), the fixed-effects model was used for the effect size combination and the results showed no statistically significant difference between the two groups (Z=1.44, P=0.15; OR, 0.68; 95% CI, 0.40-1.15). This suggested that the Ti-PEEK and PEEK groups had similar postoperative cage sedimentation rates at 6-12 months postoperatively (Fig. 3).

Comparison of postoperative ODI scores (3, 6 and 12 months). A total of four studies reported the postoperative ODI scores (3 months) between the Ti-PEEK and PEEK groups (229 patients, 118 in the Ti-PEEK group and 111 in the PEEK group). As the heterogeneity test (I^2=0%; Q-test, P=0.75) found that the heterogeneity of these studies was not statistically significant, the fixed-effects model was used for effect size combination. The meta-analysis showed a statistically significant difference between the two groups [Z=2.30; P=0.02; OR,-4.21; 95% CI, (-7.80)-(-0.62)], suggesting that the Ti-PEEK group had improved postoperative functional recovery compared with that in the PEEK group at 3 months. A total of five studies reported the postoperative ODI scores (6 months) between the Ti-PEEK and PEEK groups (372 patients, 184 in the Ti-PEEK group and 188 in the PEEK group). As the heterogeneity test (I^2=49%; Q-test, P=0.1) suggested that the heterogeneity was not statistically significant, the fixed-effects model was used to combine the effect sizes and the results showed no statistically significant difference between the two groups [Z=0.86; P=0.39; OR, -1.25; 95% CI, (-4.11)-1.61], indicating that functional recovery was comparable between the two groups at 6 months postoperatively. A total of five studies reported postoperative ODI scores (12 months) between the Ti-PEEK and PEEK groups (366 patients, 181 in the Ti-PEEK group and 185 in the PEEK group). As that the heterogeneity test (I^2=40%; Q-test, P=0.15) suggested no statistically significant heterogeneity, the meta-analysis using the fixed-effects model showed no statistically significant difference between the two groups [Z=1.18; P=0.24; OR, 1.89; 95% CI, (-1.25)-5.02)], suggesting that the functional recovery effect was comparable between the two groups at 12 months postoperatively. Combined with the aforementioned results, this suggested that the Ti-PEEK group had improved spinal stability in the short term (<3 months) and thus improved postoperative functional recovery, while the two groups converged in terms of postoperative functional recovery in the long term (>6 months; Fig. 4).

Comparison of postoperative VAS score for back pain (3, 6 and 12 months). A total of four studies reported the postoperative VAS scores for back pain (3 months) between the Ti-PEEK and PEEK groups (229 patients, 118 in the Ti-PEEK group and 111 in the PEEK group). As the heterogeneity test (I^2=75%; Q-test, P=0.008) suggested that the heterogeneity was statistically significant, meta-analysis using the random effects model showed no statistically

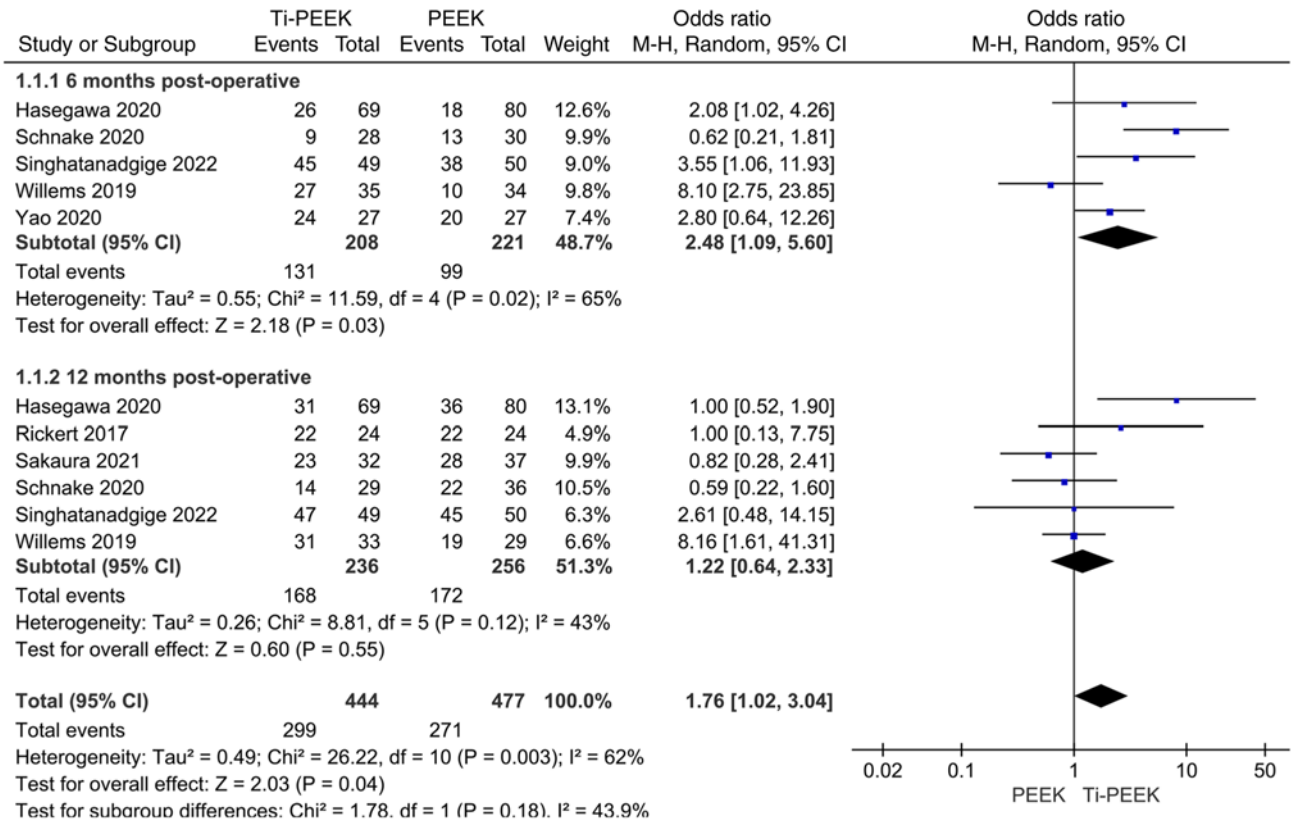

Figure 2. Forest plots of studies evaluating bone fusion rates in the Ti-PEEK vs. the PEEK group at 6 and 12 months postoperatively. Odds ratio values are shown as boxes, 95% CIs are shown as horizontal lines and the combined effect size results are shown as black diamonds. Positive effects represent higher rates of bone fusion in patients with Ti-PEEK cages placed after lumbar fusion and negative effects represent higher rates of bone fusion in patients with PEEK cages placed after lumbar fusion. Ti-PEEK, titanium coated polyetheretherketone; M-H, Mantel-Haenszel.

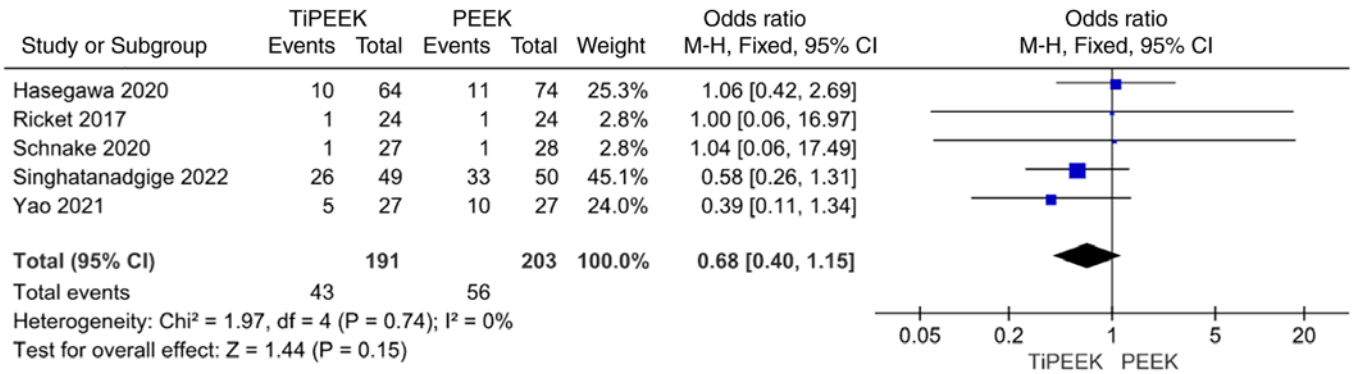

Figure 3. Forest plot of cage sedimentation rates in the Ti-PEEK group vs. PEEK group from 6-12 months postoperatively. Odds ratio values are shown as boxes, 95% CIs are shown as horizontal lines and the combined effect size results are shown as black diamonds. Positive effects represent lower cage sedimentation rates in patients with Ti-PEEK cages placed after lumbar fusion; negative effects represent lower cage sedimentation rates in patients with PEEK cages placed after lumbar fusion. Ti-PEEK, titanium coated polyetheretherketone; M-H, Mantel-Haenszel.

significant difference between the two groups [Z=0.37; P=0.71; OR, -0.15; 95% CI, (-0.96)-0.66)]. This suggested that the effect of lower back pain relief at 3 months postoperatively was comparable between the two groups. A total of four studies reported the postoperative VAS scores for back pain (6 months) between the Ti-PEEK and PEEK groups (223 patients, 115 in the Ti-PEEK group and 108 in the PEEK group). As the heterogeneity test (I^2=0%; Q-test, P=0.87) suggested that the heterogeneity was not statistically significant, meta-analysis using a fixed-effects model showed a statistically significant difference between the two groups [Z=3.34, P=0.0008; OR=-0.56; 95% CI, (-0.89)-(-0.23)], suggesting that the Ti-PEEK group had improved postoperative lower back pain symptom relief compared with that in the PEEK group at 6 months postoperatively. A total of four studies reported the postoperative VAS scores for back pain (12 months) between the Ti-PEEK and PEEK groups (221 patients, 116 in the Ti-PEEK group and 105 in the PEEK group). As the heterogeneity test (I^2=63%; Q-test, P=0.04) suggested that the heterogeneity was statistically significant,

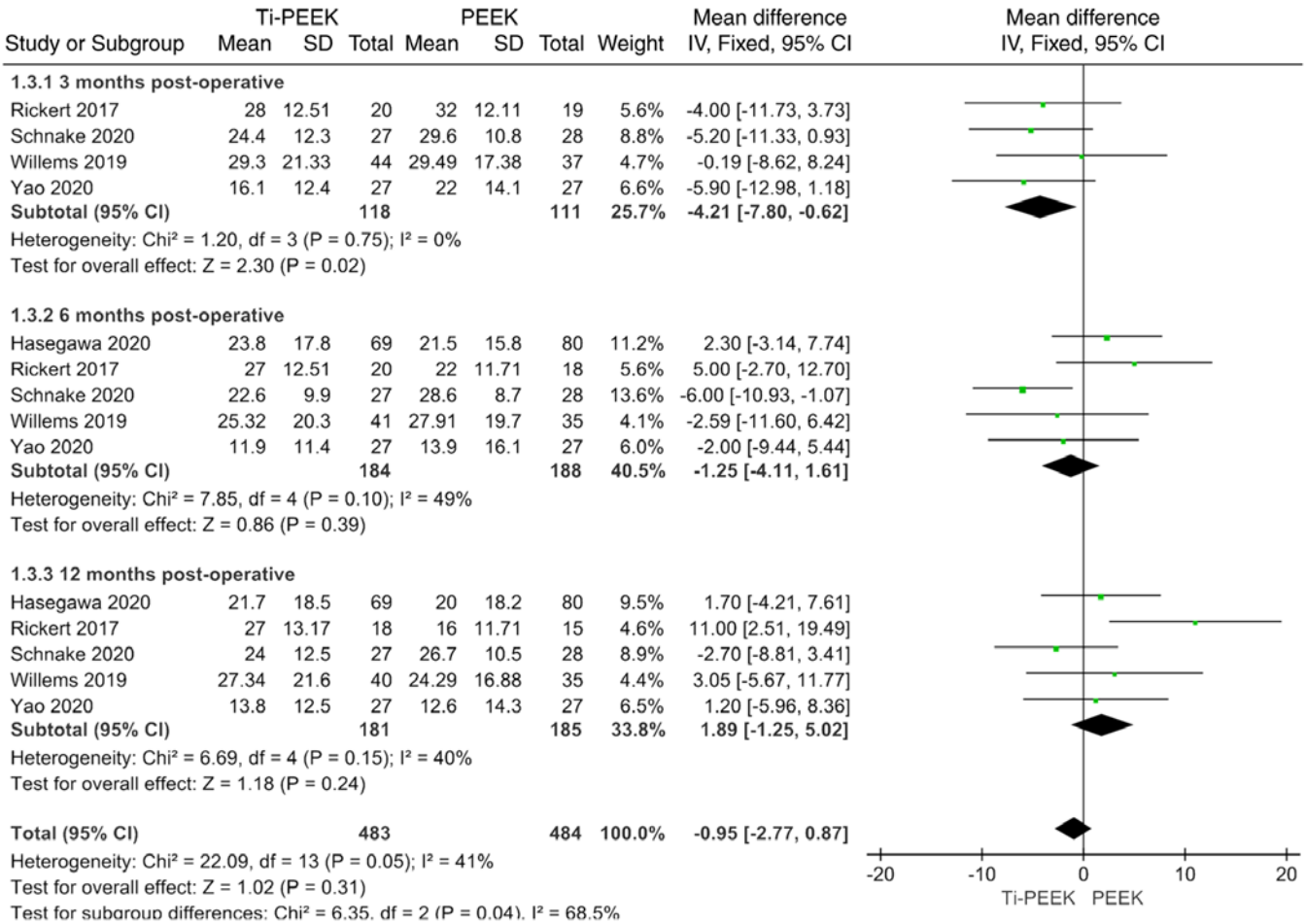

Figure 4. Forest plot of Oswestry Disability Index scores in the Ti-PEEK vs. PEEK group postoperatively (3, 6 and 12 months). Odds ratio values are shown as boxes, 95% CIs are shown as horizontal lines and the combined effect size results are shown as black diamonds. Positive effects represent better postoperative functional recovery in patients with Ti-PEEK cages placed after lumbar fusion, and negative effects represent better postoperative functional recovery in patients with PEEK cages placed after lumbar fusion. ODI, Oswestry Disability Index; Ti-PEEK, titanium coated polyetheretherketone; M-H, Mantel-Haenszel.

meta-analysis using the random effects model showed no statistically significant difference between the two groups [Z=0.11; P=0.91; OR, 0.04; 95% CI, (-0.63)-0.71)], suggesting that the Ti-PEEK and PEEK groups were similar in terms of lower back pain symptom relief at 12 months postoperatively (Fig. 5).

Publication bias and sensitivity analysis. ReviewManager 5.4 statistical software provided by the Cochrane Collaboration was used to analyze the publication bias of the four outcome indicators: i) Bone fusion rate; ii) cage subsidence rate; iii) postoperative ODI score; and iv) postoperative lower back pain VAS score. A funnel plot is provided in Fig. 6. The horizontal axis of the funnel plot is the effect size, which is related to the OR value; the smaller the OR value, the more the distribution is to the left and vice versa. The y axis is the standard error, which is related to the sample size; the larger the sample size, the higher the accuracy, and the smaller the standard error, the more the distribution is concentrated upward. The vertical median in the middle, which is perpendicular to the horizontal axis, is the combined OR value. Ideally, each study should be evenly distributed on the left and right sides of the vertical midline, with large samples concentrated at the top and small samples scattered at the bottom of the graph. The results showed that the samples were concentrated around the vertical midline and in the upper middle of the graph, with symmetry between the left and right sides, suggesting no significant publication bias (Fig. 6). After eliminating the samples with a large bias one by one through sensitivity analysis, the remaining samples were pooled for meta-analysis, and the results did not show any changes; therefore, the data of this study were considered to be relatively stable and reliable.

Discussion

The lumbar vertebrae often bear high pressure in the human body, leading to degenerative vertebral disease in the lumbar vertebrae. This occurs mainly in the lower L vertebrae (L4/5 and L5/S1) (23,24) and is often accompanied by severe degeneration and collapse of the intervertebral disc resulting in smaller local lordosis, thus affecting overall balance of the spine (25). LIF is the standard procedure used by spinal surgeons to treat various lumbar diseases. Intervertebral fusion aims to reconstruct the height and lordosis angle of the intervertebral space and achieve radiological interbody bone fusion (26). Currently, PEEK and Ti-PEEK cages are the most commonly used fusion devices in spine

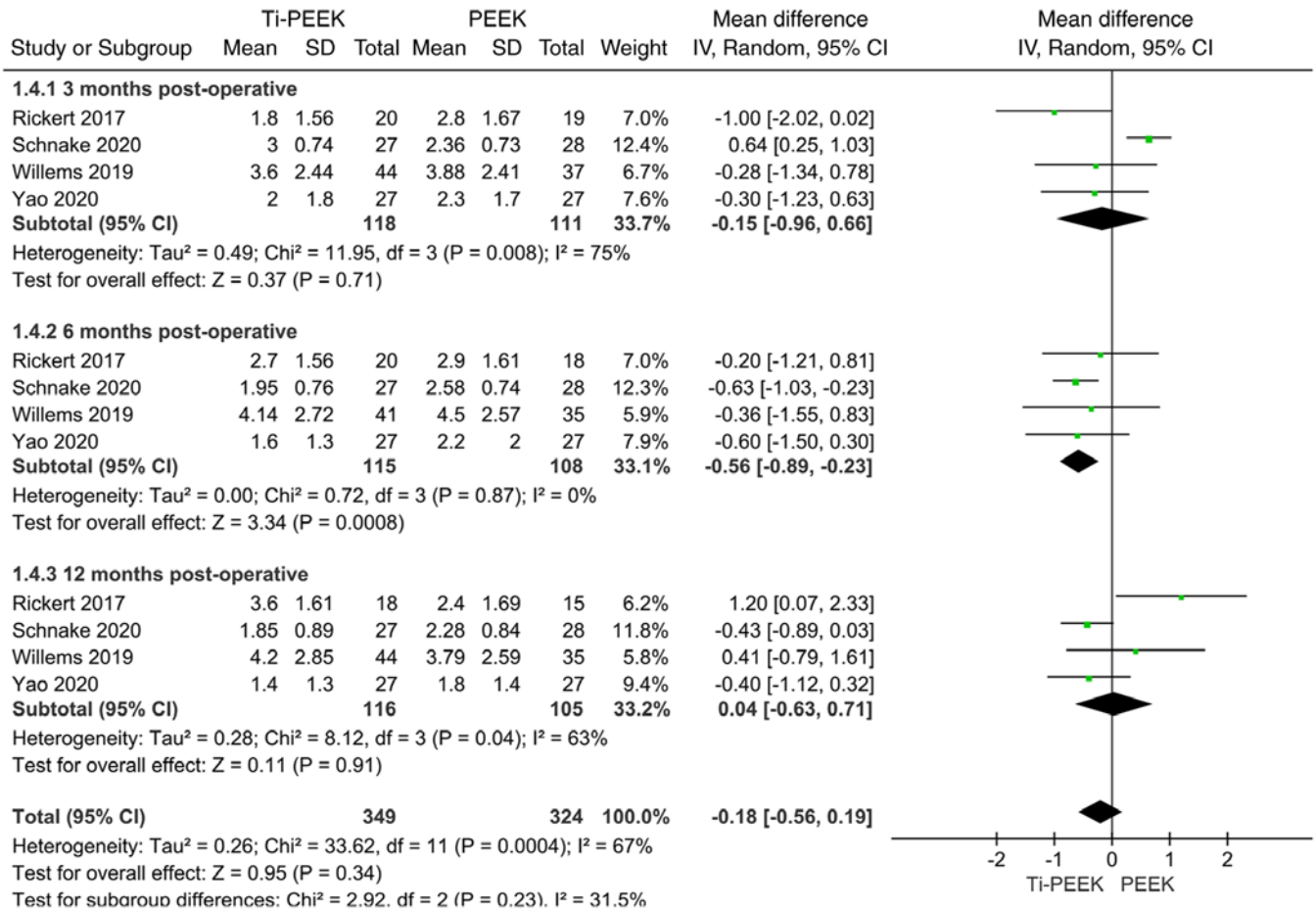

Figure 5. Forest plots of visual analog scale scores for lower back pain in the Ti-PEEK group versus the PEEK group postoperatively (3, 6 and 12 months). Odds ratio values are shown as boxes, 95% CIs are shown as horizontal lines and the combined effect size results are shown as black diamonds. Positive effects represent better postoperative lower back pain symptom relief in patients with Ti-PEEK cages placed after lumbar fusion and negative effects represent better postoperative lower back pain symptom relief in patients with PEEK cages placed after lumbar fusion. VAS, visual analog scale; Ti-PEEK, titanium coated polyetheretherketone.

surgery (27). PEEK cages have an elastic modulus similar to that of human cortical bone and good radiation penetration, which enables them to improve the evaluation of the progress of bone fusion. PEEK has been widely used for vertebral fusion in spinal surgery and is currently the most widely used fusion material (12). Based on the PEEK cage, the Ti-PEEK cage is evenly coated on the surface using low-temperature coating technology and has an elastic modulus similar to that of PEEK with improved biocompatibility and bone conductivity; therefore, it has been increasingly favored by spine surgeons (28). Therefore, the present study compared the bone fusion rate, cage settlement rate, postoperative ODI score and VAS score of lower back pain between Ti-PEEK and PEEK cages.

At present, to the best of our knowledge, only a few studies compared Ti-PEEK cages with PEEK cages and the follow-up time is limited (4,29). In the present study, the bone fusion rates were compared at 6 and 12 months after surgery. The results showed that compared with the uncoated PEEK cage, the Ti-PEEK cage showed more advantages in terms of the bone fusion rate 6 months after the operation. This indicated that compared with that achieved using uncoated PEEK cages, Ti-PEEK cages ensured improved bone growth capacity in the short term (≤6 months), which was consistent with the results of Massaad *et al* (30). Studies showed that PEEK cages form a special biofilm that affected cortical bone growth, thereby slowing down the rate of bone fusion (3,28). Ti-PEEK has no such characteristics and the surface Ti coating can provide more solid stability in the vertebral space by increasing friction to limit micromovement, while its superior cell adhesion characteristics provide a good environment for cell growth. Simultaneously, Ti-PEEK stimulates osteoblasts activity and reduces osteoclast activity, promoting early bone fusion in the surgical segment (28,31). Kashii *et al* (32) and Welsh *et al* (33) also showed through *in vitro* and *in vivo* experiments in animals that Ti or Ti-coated cages promoted osteocyte growth and surface bone tissue growth of Ti-coated cages was ~five times that of uncoated cages. However, the present study showed that there was no statistically significant difference in the bone fusion rate between the two groups at 12 months after surgery. The present results indicated that the two groups had a comparable rate of intervertebral bone fusion at 12 months after lumbar interbody fusion and the postoperative effect was similar.

The cage settlement rate, which is the opposite of the bone fusion rate during LIF, poses a challenge for spine surgeons. The elastic modulus of Ti cage material is much larger than that of human cortical bone, which leads to a

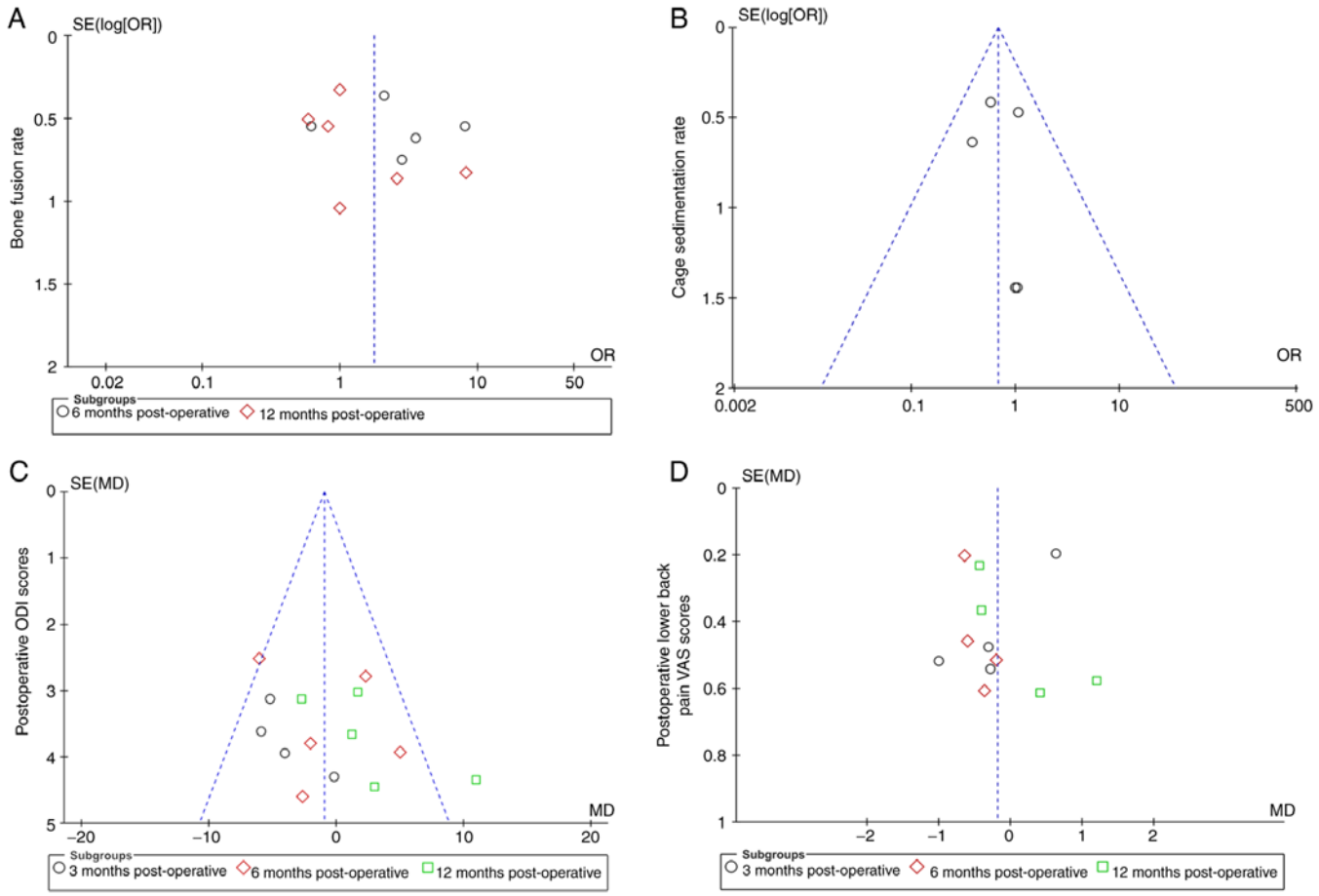

Figure 6. Funnel plot of outcome indicators. The horizontal axis is the effect size, the vertical axis is the SE and the vertical midline indicates the combined OR. Each sample is represented by a graph in the figure and the basic symmetry and concentrated distribution of samples on both sides of the vertical midline in the figure indicates the absence of significant publication bias. (A) Bone fusion rate (6 and 12 months postoperatively). (B) Cage sedimentation rate (6-12 months postoperatively). (C) Postoperative Oswestry Disability Index score (3, 6 and 12 months postoperatively). (D) Postoperative lower back pain visual analog scale scores (3, 6 and 12 months postoperatively). OR, odds ratio; MD, mean difference.

high sedimentation rate, which is one of its main disadvantages. Medical grade PEEK materials are regarded as promising alternatives because they have the same elastic modulus as human cortical bone, which is beneficial for reducing settlement rate in the cage. As a composite material, it was unclear if the Ti-PEEK cage had the same low cage settlement rate as the PEEK cage (3,32,34). The current meta-analysis compared the cage settlement rate between Ti-PEEK and PEEK cages 6 months after lumbar interbody fusion, and the results showed that there was no statistically significant difference in the settlement rate between the two groups. This indicated that the Ti coating on the PEEK surface did not change the elastic modulus of the PEEK. This result was consistent with those of Lv *et al* (4) and Massaad *et al* (30). Due to the limited follow-up of the postoperative cage sedimentation rate in the literature included in the present study, caution needs to be exercised in the assumption of the cage sedimentation rate results of the present meta-analysis.

The primary purpose of LIF is to relieve pain and achieve good functional recovery and clinical efficacy. Postoperative ODI and VAS scores are used to evaluate postoperative functional recovery and pain relief. The results of the present study showed that, compared with that of the PEEK cages, Ti-PEEK cages had a significant advantage in the ODI score at 3 months after the operation. However, there was no significant difference in the ODI scores between the two groups at 6 and 12 months postoperatively. Regarding the VAS score, Ti-PEEK cages had an advantage over PEEK cages in relieving lower back pain 6 months after surgery. However, there was no difference in the VAS scores for lower back pain between 3 and 12 months after surgery. Combining the postoperative ODI scores, lower back pain VAS scores and bone fusion rates, the results indicated that the Ti-PEEK cage could promote bone growth in the early period (≤6 months), which nay achieve improved bone fusion, and thus provide improved relief of lower back pain symptoms and postoperative functional recovery in the early period. The clinical effect of the Ti-PEEK cage in the early period (≤6 months) was improved compared with that in the PEEK group. However, the two groups had similar bone fusion rates in the long term after surgery (≥12 months), so it is reasonable that there was no significant difference in later ODI and VAS scores between the two groups.

In conclusion, both Ti-PEEK and PEEK cages had high bone fusion rates, low cage settlement rates and good clinical efficacy. However, Ti-PEEK cages provided the advantages of both Ti and PEEK. Ti-PEEK has an elastic modulus close to that of human cortical bone and promotes the growth of

osteoid cells and increases the cell adhesion space, enabling Ti-PEEK cages to achieve a higher bone fusion rate and improved relief of lower back pain in the early postoperative period without increasing the cage settlement rate, thereby obtaining improved clinical outcomes.

This meta-analysis had some limitations. First, spinal surgeons differed in their surgical methods and use of cage fillings (autologous bone, allogeneic bone or mixed fillings). Second, only seven articles were included, including four randomized controlled trials, two prospective studies and one retrospective study with a low level of evidence. Third, this limited data restricted the ability to conduct further comparisons and subgroup analyses. Fourth, the current study was based on a secondary analysis of the original literature and the relative follow-up duration of the outcome indicators adopted in the original literature that met the inclusion criteria was limited. For example, detailed data on the long-term follow-up results of the cage sedimentation rate were not provided in the original literature. Meta-analysis of the long-term postoperative cage sedimentation rates could not be performed. However, with an increase in study sample size, extension of the follow-up and an improvement in the quality of the included samples, the conclusions obtained from the present meta-analysis could be further validated and supported.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Not applicable.

Authors' contributions

SL and XL participated in the design of this study and performed the statistical analysis. XB and YW performed the study and collected data. PH and HL conceived the study, interpreted data and drafted the manuscript. All authors have read and approved the final manuscript. SL and XL confirm the authenticity of all the raw data.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Resnick DK, Choudhri TF, Dailey AT, Groff MW, Khoo L, Matz PG, Mummaneni P, Watters WC III, Wang J, Walters BC, *et al*: Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 12: Pedicle screw fixation as an adjunct to posterolateral fusion for low-back pain. J Neurosurg Spine 2: 700-706, 2005.
2. de Kunder SL, Rijkers K, Caelers IJMH, de Bie RA, Koehler PJ and van Santbrink H: Lumbar interbody fusion: A historical overview and a future perspective. Spine (Phila Pa 1976) 43: 1161-1168, 2018.
3. Verma R, Virk S and Qureshi S: Interbody fusions in the lumbar spine: A review. HSS J 16: 162-167, 2020.
4. Lv ZT, Xu Y, Cao B, Dai J, Zhang SY, Huang JM, Liang S and Jiang FX: Titanium-coated PEEK versus uncoated PEEK cages in lumbar interbody fusion: A systematic review and meta-analysis of randomized controlled trial. Clin Spine Surg: Aug 24, 2022 (Epub ahead of print).
5. Su EP, Justin DF, Pratt CR, Sarin VK, Nguyen VS, Oh S and Jin S: Effects of titanium nanotubes on the osseointegration, cell differentiation, mineralisation and antibacterial properties of orthopaedic implant surfaces. Bone Joint J 100-B: 9-16, 2018.
6. Li C, Liao Z, Zhu J, *et al*: Structure and materials of lumbar interbody fusion apparatus. Int J Orthop 38: 360-363, 2017.
7. Ma R and Tang T: Current strategies to improve the bioactivity of PEEK. Int J Mol Sci 15: 5426-5445, 2014.
8. Mobbs RJ, Phan K, Assem Y, Pelletier M and Walsh WR: Combination Ti/PEEK ALIF cage for anterior lumbar interbody fusion: Early clinical and radiological results. J Clin Neurosci 34: 94-99, 2016.
9. Olivares-Navarrete R, Hyzy SL, Slosar PJ, Schneider JM, Schwartz Z and Boyan BD: Implant materials generate different peri-implant inflammatory factors: Poly-ether-ether-ketone promotes fibrosis and microtextured titanium promotes osteogenic factors. Spine (Phila Pa 1976) 40: 399-404, 2015.
10. Setzer M, Eleraky M, Johnson WM, Aghayev K, Tran ND and Vrionis FD: Biomechanical comparison of anterior cervical spine instrumentation techniques with and without supplemental posterior fusion after different corpectomy and discectomy combinations: Laboratory investigation. J Neurosurg Spine 16: 579-584, 2012.
11. Nemoto O, Asazuma T, Yato Y, Imabayashi H, Yasuoka H and Fujikawa A: Comparison of fusion rates following transforaminal lumbar interbody fusion using polyetheretherketone cages or titanium cages with transpedicular instrumentation. Eur Spine J 23: 2150-2155, 2014.
12. Seaman S, Kerezoudis P, Bydon M, Torner JC and Hitchon PW: Titanium vs polyetheretherketone (PEEK) interbody fusion: Meta-analysis and review of the literature. J Clin Neurosci 44: 23-29, 2017.
13. Han CM, Lee EJ, Kim HE, Koh YH, Kim KN, Ha Y and Kuh SU: The electron beam deposition of titanium on polyetheretherketone (PEEK) and the resulting enhanced biological properties. Biomaterials 31: 3465-3470, 2010.
14. Hasegawa T, Ushirozako H, Shigeto E, Ohba T, Oba H, Mukaiyama K, Shimizu S, Yamato Y, Ide K, Shibata Y, *et al*: The titanium-coated PEEK cage maintains better bone fusion with the endplate than the PEEK cage 6 months after PLIF surgery: A multicenter, prospective, randomized study. Spine (Phila Pa 1976) 45: E892-E902, 2020.
15. Rickert M, Fleege C, Tarhan T, Schreiner S, Makowski MR, Rauschmann M and Arabmotlagh M: Transforaminal lumbar interbody fusion using polyetheretherketone oblique cages with and without a titanium coating: A randomised clinical pilot study. Bone Joint J 99-B: 1366-1372, 2017.
16. Sakaura H, Ikegami D, Fujimori T, Sugiura T, Yamada S and Mukai Y: Surgical outcomes after posterior lumbar interbody fusion using traditional trajectory screw fixation or cortical bone trajectory screw fixation: A comparative study between the polyetheretherketone cage and the same shape titanium-coated polyetheretherketone cage. Clin Neurol Neurosurg 209: 106945, 2021.
17. Schnake KJ, Fleiter N, Hoffmann C, Pingel A, Scholz M, Langheinrich A and Kandziora F: PLIF surgery with titanium-coated PEEK or uncoated PEEK cages: A prospective randomised clinical and radiological study. Eur Spine J 30: 114-121, 2021.

18. Singhatanadgige W, Tangchitcharoen N, Kerr SJ, Tanasansomboon T, Yingsakmongkol W, Kotheeranurak V and Limthongkul W: Comparison of PEEK and TiPEEK in minimally invasive transforaminal lumbar interbody fusion: A randomized clinical trial. World Neurosurg 68, 2022.
19. Willems K, Lauweryns P, Verleye G and VAN Goethem J: Randomized controlled trial of posterior lumbar interbody fusion with Ti- and CaP-nanocoated polyetheretherketone cages: Comparative study of the 1-year radiological and clinical outcome. Int J Spine Surg 13: 575-587, 2019.
20. Yao YC, Chou PH, Lin HH, Wang ST and Chang MC: Outcome of Ti/PEEK versus PEEK cages in minimally invasive transforaminal lumbar interbody fusion. Global Spine J 13: 472-478, 2023.
21. Higgins JPT, Altman DG, Gøtzsche PC, *et al*.: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 343: d5928, 2011.
22. Stang A: Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 25: 603–605, 2010.
23. Rade, M, Määttä JH, Freidin MB, Airaksinen O, Karppinen J and Williams FMK: Vertebral endplate defect as initiating factor in intervertebral disc degeneration: Strong association between endplate defect and disc degeneration in the general population. Spine (Phila Pa 1976) 43: 412-419, 2018.
24. Hey HWD, Lau ET, Tan KA, Lim JL, Choong D, Lau LL, Liu KG and Wong HK: Lumbar spine alignment in six common postures: An ROM analysis with implications for deformity correction. Spine (Phila Pa 1976) 42: 1447-1455, 2017.
25. Barrey C, Jund J, Noseda O and Roussouly P: Sagittal balance of the pelvis-spine complex and lumbar degenerative diseases. A comparative study about 85 cases. Eur Spine J 16: 1459-1467, 2007.
26. Lee JH, Lee JH, Yoon KS, Kang SB and Jo CH: Comparative study of unilateral and bilateral cages with respect to clinical outcomes and stability in instrumented posterior lumbar interbody fusion. Neurosurgery 63: 109-114, 2008.
27. Fang S and Zeng Z: Research progress of bone grafting material in interbody fusion. J Spinal Surg 16: 57-61, 2018.
28. Wu X, Liu X, Wei J, Ma J, Deng F and Wei S: Nano-TiO2/PEEK bioactive composite as a bone substitute material: In vitro and in vivo studies. Int J Nanomedicine 7: 1215-1225, 2012.
29. Assem Y, Mobbs RJ, Pelletier MH, Phan K and Walsh WR: Radiological and clinical outcomes of novel Ti/PEEK combined spinal fusion cages: a systematic review and preclinical evaluation. Eur Spine J 26: 593–605, 2017.
30. Massaad E, Fatima N, Kiapour A, Hadzipasic M, Shankar GM and Shin JH: Polyetheretherketone versus titanium cages for posterior lumbar interbody fusion: Meta-analysis and review of the literature. Neurospine 17: 125-135, 2020.
31. Gittens RA, McLachlan T, Olivares-Navarrete R, *et al*. The effects of combined micron-/submicron-scale surface roughness and nanoscale features on cell proliferation and differentiation. Biomaterials 32: 3395–3403, 2011.
32. Kashii M, Kitaguchi K, Makino T and Kaito T: Comparison in the same intervertebral space between titanium-coated and uncoated PEEK cages in lumbar interbody fusion surgery. J Orthop Sci 25: 565-570, 2020.
33. Walsh WR, Pelletier MH, Christou C, He J, Vizesi F and Boden SD: The in vivo response to a novel Ti coating compared with polyether ether ketone: Evaluation of the periphery and inner surfaces of an implant. Spine J 18: 1231-1240, 2018.
34. Chong E, Mobbs RJ, Pelletier MH and Walsh WR: Titanium/Polyetheretherketone Cages for Cervical Arthrodesis with Degenerative and Traumatic Pathologies: Early Clinical Outcomes and Fusion Rates. Orthop Surg 8: 19–26, 2016.