Comparison between Titanium and Polymer Interbody Cages in Spinal Fusion Surgery: A Review of Clinical Studies

Abstract

In recent years, spinal fusion surgery has become one of the most common treatments for spinal cord injuries, while the interbody cages, which replace the damaged interbody discs in the surgeries, have undergone extensive changes in design and material. These changes are quite visible, ranging from plain titanium cages made using the conventional manufacturing methods to customized porous titanium cages, which are made using additive manufacturing technology, or titanium-coated polymer cages. Among all the materials used in manufacturing the interbody cages, PolyEther Ether Ketone (PEEK) and titanium are the most common ones. Each of these two has its own advantages and disadvantages. Several studies have compared these two materials, mostly based on the two characteristics of subsidence and fusion rates. The present study performed a comprehensive review of the published clinical studies comparing the titanium and PEEK cages in order to make a comprehensive evaluation of these two. According to the reviewed studies, both materials had relatively similar results in subsidence rate, with no significant difference. However, it was shown that the titanium cages had a better fusion rate and subsequently were more likely to be successful in the clinical settings than the PEEK cages.

Keywords: Spine, Titanium, Spinal fusion, Total Disc Replacement, Polymers

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Introduction

It has been more than six decades that posterior and anterior spinal fusion surgeries for spinal disorder treatment have been introduced. The procedure is an effective therapeutic method to stabilize the damaged area of the spine. It reduces the pressure on different spinal components and soft tissue, restores the spinal curvature, and corrects the anatomical abnormalities [3, 4]. The common spinal fusion procedures include the Anterior Cervical Discectomy and Fusion (ACDF) [5, 6], Posterior Lumbar Interbody Fusion (PLIF) [7], and Transforaminal Lumbar Interbody Fusion (TLIF) [8], which are performed to treat various spinal disorders, such as canal stenosis, vertebral slippage, and disc herniation [9]. In the beginning, these procedures were performed using different bone grafts to connect the vertebras and maintain the integrity between them [1, 2]. However, since about 40 years ago, the application of interbody cages in these surgeries has become more common because the individual bone grafts caused various complications, leading to poor and incomplete fusion or even displacement [10]. It has been estimated that, on average, more than 400,000 spinal fusion surgeries are performed annually in the United States [11], of which about 200,000 are on the lumbar area, while about 150,000 cases are on the cervical area [11]. Moreover, it has been reported that about 83% of the surgeries on degenerated disks are performed with the help of interbody cages [12].

As one of the most common materials used in implant manufacture, titanium is widely used in orthopedic and maxillofacial surgeries due to its favorable biocompatibility and mechanical properties [13, 14]. Therefore, the use of titanium as the main material for interbody cages has been increasing in recent years, while the related designs have changed significantly over the years. According to studies, titanium interbody cages are safe and effective and have a high successful fusion rate [15].

However, after these titanium cages became popular, the attention turned to other available materials for these implants. Various samples were produced, with carbon fiber cages being one of the most important. These cages have shown a relatively good fusion rate in clinical studies and can be a good option for cervical and lumbar surgeries due to their strength (16, 17). The interbody cages usually cause imaging artifacts, leading to an increased error rate and difficulty in diagnosis. Therefore, several studies have compared the interbody cages made from different materials in terms of artifacts created in CT scan and MRI images, and it has been found that carbon-fiber-reinforced polymer cages had more favorable results compared with titanium cages (18).

The titanium cages have some other limitation as well, including the possibility of cage subsidence in the vertebral body, difficulty in detecting the successful fusion in radiographic images due to the radio-opacity of titanium, and the high modulus of elasticity, which results in the stress shielding phenomenon, leading to the reduction of the load exerted on the tissue and delayed or defective bone regeneration and fusion (19). These limitations led to the development of a new polymer material, the Polyether Ether Ketone (PEEK). The modulus of elasticity for PEEK is close to that of the bone, eliminating the problem of stress shielding caused by titanium. Moreover, PEEK is radiolucent, so it was very successful (20). In general, titanium alloy and PEEK both have their own advantages and disadvantages. However, both are biocompatible. Therefore, the idea of titanium-coated polymer interbody cages was raised. Moreover, the idea of interbody cages coated with ceramics, such as tri-calcium phosphate, hydroxyapatite, etc., was investigated and yielded various results.

Overally, these coated cages had a high fusion rate and low rates of failure and safety problems (21). Also, according to studies, titanium-coated cages had better results and were safer than bone grafts. Over time, many creative ideas were proposed for titanium cage designs, some of which were more effective and showed better results. For example, titanium cervical cages with a Z-shaped design showed acceptable clinical results (23). These titanium cage designs were investigated by various software and simulation studies to find the fusion and subsidence rates (24). A study evaluated the hydroxyapatite-coated interbody cages made from PEEK and found that these cages had significantly increased adhesion, so they could be used for various orthopedic and spinal surgeries (25).

Moreover, another study on a titanium-coated PEEK cage using the electron beam method showed that the coated cages had higher bone coverage and integrity than the cages without a coating layer. Thus, the coated cages could be a good alternative to polymer cages (26). Recently, the titanium-coated cages made from PEEK using different techniques have received much attention. For example, the VPS-coated composite cages used for coating the titanium on PEEK or carbon cages showed acceptable clinical results and had a high rate of successful fusion (27). Another study showed a high fusion rate and low subsidence rate one year after the spinal fusion surgeries using titanium-coated PEEK cages, which was clinically acceptable (28).

In recent years, additive manufacturing technology has significantly facilitated several production challenges and gave us the feature of implant personalization. Consequently, the application of this technology in interbody cage manufacture has also been developed. Using these methods, porous titanium cages were introduced to the market. These cages were made by the 3D-printing devices that make integrated porosities of specific and identical sizes, which can improve the bone growth process and accelerate the fusion. The stiffness properties of these porous networks are closely similar to the mechanical properties of the bone. These 3D-printed cages showed acceptable biocompatibility and fusion, so they can be used extensively (29). According to clinical studies, porous titanium cages had a lower subsidence rate in post-operative follow-ups compared to the PEEK cages [30].

Another feature of additive manufacturing technology is personalization, which has received considerable attention in the field of implants. Using this feature, implants can be personalized for each patient, with specific anatomical dimensions and sizes. These customized titanium implants can be a suitable alternative to the current titanium and PEEK cages [31]. The different cage types discussed above are presented in Table 1 with the relevant commercial examples.

Given the various designs for interbody cages and the raw materials used for their manufacture, several studies have investigated the different features of these implants. Regarding the titanium and PEEK as the main materials used for cage manufacture, a comprehensive clinical comparison is needed to further illustrate their main parameters, including the subsidence rate in the vertebral body [32] and the fusion rate [33]. Therefore, the present study intended to make a comprehensive review of the literature in this field and summarize the latest findings of clinical studies in order to help orthopedic surgeons and neurosurgeons.

Table 1- Samples of the interbody cages introduced in different groups by the manufacturing companies in recent years.

Titanium cages	Carbon fiber cages	PEEK cages	Ti-coated PEEK cages	3D printed Ti cages
Tezo  Ulrich medical [37]	 ETurn Icotec-Medical [36]	Aleutian  Stryker/k2m [35]	PROTI 360  DePuy Synthes [34]	 CONDUIT DePuy Synthes [34]
 Ti CAPSTONE Medtronic [38]	 CONCORDE DePuy Synthes [34]	 PEEK CAPSTONE Medtronic [38]	 CAPSTONE PTC Medtronic [38]	 Adaptix Medtronic [38]
 TITAN ENDOSKELETON TC Medtronic [38]	 BENGAL DePuy Synthes [34]	 PEEK CORNERSTONE Medtronic [38]	 CORNERSTONE PTC Medtronic [38]	 TrellOss™-C Zimmer Biomet [39]

Comparisons between titanium and PEEK cages using clinical results

Numerous studies have been published on interbody cages, comparing different cage types in terms of different features. In the present review, we evaluated 180 related studies, of which 53 studies on the cervical and lumbar cages were selected. Then, the study subject of comparison between the titanium and PEEK cages was selected. Finally, 13 studies were included in the study. These studies had exclusively compared the titanium and PEEK cages, or carbon-reinforced and titanium-coated cages in certain cases, and reported the post-operative results in the medium- and long-term. The present study was mainly focused on the two variables of fusion rate and subsidence rate, which have been studied clinically in post-operative follow-ups.

The first study was conducted in Germany during 2008-2013. Forty participants, including 23 female and 17 male patients with the mean age of 66, underwent lumbar fusion surgery using the PLIF method and titanium or PEEK interbody cages. Titanium cages were used for 15 patients, while 25 received PEEK cages. No bone grafts were used in the patients. The patients underwent post-operative follow-up using the CT scan. Moreover, the successful fusion was considered as at least 3 connected parts fused together. Also, the authors developed a new scoring system for fusion evaluation. The study showed a low fusion rate in both groups due to the lack of bony grafts, and no case of cage subsidence was reported. Finally, the authors concluded that bone grafts should be used in combination with interbody cages if possible to increase the chance of successful fusion [(40).]

Another clinical study in Japan during 2016-2018 compared the PEEK cages with and without titanium coating in the rate of successful fusion. The study included 149 participants, including 84 male and 65 female patients with the mean age of 67, undergoing PLIF surgery in one level. The PEEK cages with and without titanium coating were used for 80 and 69 participants, respectively. The patients were followed using the CT scan within 12 months post-surgery. In the 6-month follow-up, the group receiving titanium-coated PEEK cages had a relatively higher rate of endplate fusion compared to another group. Therefore, it can be concluded that titanium-coated PEEK cages were better than PEEK cages without coating in fusion rate. Moreover, both groups showed significant improvements using the ODI and JOABPEQ indices in the 12-month follow-up, with no significant inter-group difference in cage subsidence rate and screw loosening. However, only 45% of the patients had a complete fusion in the 12-month follow-up. These poor results can be explained by the relatively strict criteria used for defining the successful fusion. According to the criteria, the patients were classified into 3 groups in terms of fusion status, and a complete fusion was defined as the formation of a bony integration between the bodies of the adjacent vertebrae [(41).]

Another clinical study by a German team in 2012 compared the PEEK cages with and without titanium coating. The study included 40 patients that underwent fusion surgery using the TLIF method and were followed using the CT scan for 12 months. Half of the patients received PEEK cages without titanium coating, while the rest received the titanium-coated PEEK cages. The subsidence was defined as more than 1 mm of height reduction between the vertebrae alongside the visible cracks on the endplates, while the fusion was defined as the presence of a bony bridge connection between the two parts. According to the findings, no significant inter-group difference was found in fusion and subsidence rates using the ODI and VAS indices. Both groups showed acceptable fusion rates and no case of subsidence [(42).]

Another clinical study on Chinese patients during 2002-2004 compared the titanium and PEEK cages. The study included 60 patients that underwent cervical fusion surgery and were followed using plain radiography for 7 years. 29 patients received titanium cages, while 31 received PEEK cages. The subsidence was defined as more than 3 mm of height reduction between the vertebrae. Moreover, fusion was defined by the three following variables: the absence of spinous process movement in the lateral radiographs, the absence of gaps between the endplates and bone grafts, and the presence of a continuous bony connection between the endplates and bone grafts. Using the JOA and NDI indices, it was found that both groups had a fusion rate of 100%, while the subsidence rate was significantly lower in the PEEK group than the titanium group. The authors concluded that PEEK cages had better results in cervical fusion surgeries than titanium cages (43).

Another study in Japan during 2008-2011 compared the titanium and PEEK cages. The study included 48 patients that underwent fusion surgery using the TLIF method and were followed using the CT scan for 24 months. 25 patients received the PEEK cages, while 23 received the titanium cages. The subsidence was defined as more than 2 mm of cage depression in the adjacent vertebrae, while the fusion was defined as the presence of a bony connection around the cage that could be observed on both sagittal and coronal planes in CT scan. After the 24-month follow-up, it was found that the group receiving titanium cages had a fusion rate of 100%, while it was 76% for the group receiving PEEK cages. Moreover, the subsidence rates were 35% and 28% in the titanium and PEEK groups, respectively (44).

Another study in Taiwan during 2002-2004 compared the titanium cages, PEEK cages, and bone grafts. The study included 55 patients that underwent cervical anterior surgery and were followed using plain radiography for 12 months. 27 patients received titanium cages, 9 received PEEK cages, and 19 patients received only bone grafts. The fusion was defined as the formation of a bony connection throughout the segment. After a 12-month follow-up, the subsidence rate was 25% in the titanium group, while there was no case of subsidence in other groups. Moreover, the fusion rate was 46% in the titanium group, while it was 100% in the groups using PEEK cages and bone grafts. The authors concluded that PEEK cage application was a suitable alternative to other methods and recommended using these cages in the cervical area (45).

As a relatively novel method for fusion surgeries, LLIF has attracted a great deal of attention. A study in the United States that was published in 2020 compared the titanium and PEEK and cages. The study included 113 patients with a mean age of 60 who underwent fusion surgery in 2017 using the LLIF method and were under clinical follow-up for 12 months. 56 patients received titanium cages, while 57 received PEEK cages. The subsidence was graded on a 3-point scale based on a pre-validated scoring system. According to the findings, the titanium group had better results than the PEEK group in terms of subsidence rate (?).

A clinical study in Japan published in 2019 compared the titanium-coated and uncoated PEEK cages made using the plasma spray technique. The study included 26 patients who underwent fusion surgery in one level during 2016-2018 using the PLIF method and were under follow-up using CT scan and functional radiography images for 12 months. The patients received either uncoated or titanium-coated PEEK cages. No case of subsidence was reported in both groups, while the total fusion rate was 88%.

Complete fusion was defined by fulfilling all the following criteria: the presence of a continuous bony bridge in the disk space in CT images, no screw loosening in CT images, no visible area surrounding the cage in radiography or CT images, and more than 3 degrees variation in the angle of the fused body in the functional images. According to CT images, bone growth and tissue formation were slightly higher in the titanium-coated cages than in the uncoated cages. The authors concluded that titanium-coated PEEK cages had a higher fusion rate and improved clinical outcomes (47).

A clinical study in Italy during 2015-2016 compared the titanium and PEEK cages. The study included 40 patients who underwent TLIF surgery and were followed for 12 months using the CT scan and certain questionnaires. Half of the patients, who had a mean age of 48, received PEEK cages, while the rest, who has a mean age of 55, received titanium cages. Fusion was scored based on a criteria suggested by Christensen et al. (48). Complete fusion was considered as a continuous bony connection in each direction. After the follow-up period, the groups did not have functional differences. Moreover, the fusion rates were 40% and 15% for the titanium and PEEK groups, respectively. Therefore, the titanium cages had better results in the fusion rate than the PEEK cages [49].

A clinical study in Japan during 2015-2016 compared the titanium-coated PEEK cages and carbon PEEK cages. The study included 126 patients who underwent PLIF surgery and were followed for 12 months using the CT scan. 92 patients received carbon PEEK cages, while 36 received titanium-coated PEEK cages. Fusion was defined as a complete bony connection between the vertebrae and bone graft in the cage and no screw loosening or vertebral movement in the functional images. A fusion stability grading was also defined in the study. Moreover, subsidence was defined as a more than 2 mm depression of the cage in the adjacent vertebral body. After the follow-up period, both groups had similar fusion rates with no significant differences, while the subsidence rate was lower in the titanium-coated group, so this group had more favorable results [50].

A clinical trial in Germany compared the titanium and PEEK cages. The study included 419 patients who underwent TLIF surgery and were followed for 50 months using the CT scan. 323 patients received PEEK cages, while 96 received titanium cages. According to the findings, there was no difference between the groups in terms of fusion rate, side effect, or integrity. However, the main goal of the mentioned study was investigating the sagittal spinal balance [51].

Due to the development in cage production, various and innovative designs have been introduced so far. For example, a titanium cage with a Z-shaped design has been introduced to the market. A clinical study in China in 2020 compared these new, Z-shaped titanium cages with PEEK cages. The study included 10 patients who underwent TLIF surgery and were followed for 3 months. 6 patients received PEEK cages, while 4 received Z-shaped titanium cages. Complete fusion was defined as an angle change of fewer than 5 degrees in the fused segment, while subsidence was defined as more than 2 mm of changes in the height between the vertebrae in radiography. The post-operative pain was assessed using the Visual Analog Scale (VAS) and the Oswestry Disability Index (ODI). According to the findings, the groups were not different in pain; however, the subsidence rate was 42% in the PEEK groups, while 0% in the Z-shaped titanium group. Moreover, the fusion rates were 67% and 100% in the PEEK and Z-shaped titanium groups, respectively. Therefore, the Z-shaped titanium cages were significantly better than the PEEK cages in fusion and subsidence [52].

A study in Germany in 2020 compared the titanium-coated and uncoated PEEK cages. The study included 60 patients who underwent PLIF surgery at one or two levels and were under clinical follow-up for 24 months. 28 patients received uncoated PEEK cages, while 27 received titanium-coated PEEK cages. 55 patients, including 36 female and 19 male patients, ended the follow-up period. The patients were evaluated using radiography and CT scan at 6, 12, and 24 months post-surgery. Fusion was defined as the presence of a continuous bony bridge between the endplates of each vertebra with the adjacent vertebrae through the cage, while subsidence was defined as more than 3 mm of any cage movement or displacement. According to the findings, there was no significant inter-group difference in the fusion and subsidence rates, and both groups had acceptable results [53].

In the studies reviewed, a total of 1234 participants were investigated, of which 270 had titanium cages, 741 had PEEK cages, and 179 had titanium-coated PEEK cages. The mean follow-up period was 24.3 months. Moreover, 145 patients were evaluated using plain radiography, while 736 were evaluated using CT scan. 353 patients were evaluated using both methods. Also, 135 patients received only the cages, while 1099 had other spinal implants combined with the cages.

A summary of the findings by the mentioned studies is presented in Table 2.

Table 2 - Comparison of the important features and results of reviewed articles

number	Number of patients	Follow-up period of patients (months)	Type of image evaluation	Definition of subsidence criteria	Definition of fusion criteria	conclusion	reference
1.	40	33	CT SCAN	It did not happen	The continuous bridge of the bone with at least 3 connected parts is considered as a fused part. A scoring system is also defined to determine the fusion rate.	There is no significant difference between titanium cage and PEEK. the reason for the weakness in the fusion is not using bone graft.	(40)
2.	149	12	CT SCAN	Cage depression more than one millimeter in the vertebrae	To define fusion, three degrees are defined, complete fusion is a continuous bony connection between the body of adjacent vertebrae.	The use of PEEK cages with titanium coating has a better fusion rate than PEEK cages.	(41)
3.	40	12	CT SCAN	Decrease in height between vertebrae more than one millimeter with cracks visible on the endplate	Presence or absence of bone connection between the two parts	Both groups showed acceptable fusion rates and no cage subsidence was observed in any of the cases.	(42)
4.	80	99	X RAY RADIOGRAPHY	Decreased height between vertebrae more than 3 mm	Absence of spinous process movement in lateral radiographic images, no distance between bone graft and end plates in images, no continuous bone connection in end plate and bone graft	Cage subsidence is much lower in the PEEK group than in the titanium group, in both groups the fusion rate is 100%.	(43)
5.	48	24	CT SCAN	Cage depression in adjacent vertebrae more than two millimeters	There is a bony connection surrounding the cage that is visible on both the sagittal plate and the coronal planes of the CT scan.	100% of the group who received the titanium cage had complete fusion, while the other group experienced only 76% success in fusion rate. Cage subsidence occurred in the titanium group by 35% and in the PEEK group by 28%	(44)
6.	55	12	X RAY RADIOGRAPHY	No exact definition provided	The formation of bony connections throughout the segment	Cage subsidence with 25% has been seen only in the titanium group and no other complications have been reported in the other two groups. Also, the fusion rate after 12 months was reported to be 46% in the titanium cage group and 100% in the other two groups of PEEK cage and bone grafts.	(45)
7.	113	12	X RAY RADIOGRAPHY /CT SCAN	Three grades according to the pre-validated system (54)	No exact definition provided	The subsidence rate in the group that used the titanium cage is more favorable than the group that used the PEEK cage.	(46)
8.	52	12	X RAY RADIOGRAPHY /CT SCAN	It did not happen	1 .continuous bony bridge in disk space in CT scan 2. No screw loosening in CT scan 3 .No visible area surrounding the cage in radiography or CT scan 4. more than 3 degrees Change in the angle of in the fused body in the functional images	The use of titanium coated PEEK cages can be effective in fusion rate and better clinical results	(47)
9.	40	12	CT SCAN	No exact definition provided	According to Christensen et al. (48), the possibility of three degrees of fusion is defined. a complete and continuous bony connection in each direction is considered fusion.	After one year, the fusion rate is reported to be 40% for the titanium group and only 15% for the PEEK group.	(49)
10.	128	12	MPR-CT/CT SCAN	Depression more than 2 mm in the adjacent vertebrae body	Complete bony connection between the vertebrae and the bone graft in the cages with no loosening of the screws or movement of the vertebrae in functional images	Both groups showed the same fusion rate, but the subsidence rate was lower in the titanium group and had better results.	(50)
11.	419	50	CT SCAN	No exact definition provided	No exact definition provided	The type of cage did not affect the fusion rate or side effects or integrity of the segment.	(51)
12.	10	3	X RAY RADIOGRAPHY	Height changes over 2 mm	The angular changes of the segment should be less than 5 degrees	Higher fusion rate and lower subsidence rate in titanium cages	(52)
13.	60	24	X RAY RADIOGRAPHY /CT SCAN	3 mm Displacement of the cage and above	Existence of complete bony connection of the end plates of each vertebrae with the adjacent vertebrae through the cage	Both types of cages have shown acceptable results	(53)

Discussion

At first, we will discuss the evolutionary course of the design and structure of interbody cages in recent decades. The related studies were reviewed to illustrate the strengths and weaknesses of the cages made of different materials, such as titanium, PEEK, and carbon fiber cages, titanium-coated PEEK cages, and titanium cages made by additive manufacturing methods. The two main materials of titanium and PEEK, which are the materials most extensively used for cage manufacture, were selected, and the main objective of the present study was to compare these two cages. We reviewed the previous clinical studies and found that they had controversial results. Therefore, we intended to have a complete review of the clinical properties of these two cages to make a proper comparison in order to help the healthcare professionals and surgeons.

The included clinical studies were those investigating the lumbar and cervical fusion surgeries with anterior or posterior approaches. The variables studied included the fusion rate, subsidence rate, patient pain index, sagittal alignment, range of motion, and other variables. Our focus was on the two main variables of fusion and subsidence rate, as well as the potential complications because if the two factors of successful fusion and lack of subsidence are not achieved, revision surgery will be needed to remove the used implant. Therefore, the risk of infection and other complications will increase [(55).] Moreover, the risk of Adjacent Surface Degeneration (ASD) in the adjacent vertebrae increases, leading to interbody disc degeneration at the adjacent levels and thus increasing the number of segments requiring surgery in the future [(56).]

We tried to include the clinical trials investigating both cervical and lumbar surgeries. Moreover, there was an acceptable geographical distribution because the studies were conducted in different parts of Europe, Asia, and the Americas. Also, the follow-up durations were quite sufficient, two years on average, so the results were reliable. The included studies had various sample sizes and yielded different and controversial results.

The main limitation of the present study was the differences in the definitions used for fusion and subsidence in the studies included. This difference in criteria could affect the final results. Also, there was a lack of conclusive and firm results in the included studies. Therefore, there is a need for more extensive clinical studies with more stringent variables.

According to our review, titanium and PEEK cages are not different in the subsidence rate. They both showed acceptable and similar results in subsidence with no significant difference. In terms of the most important variable, fusion rate, there were controversial results. However, generally, titanium cages were better than the PEEK cages in the fusion rate. This conclusion can be generalized to the cages made by additive manufacturing techniques and also coated cages. Nowadays, big companies are focusing on the porous titanium cages made by additive manufacturing methods. This area has received more attention because titanium cages have proved their capabilities. Moreover, there has been an increasing trend in the development of additive manufacturing technology. There have been studies on the production of porous titanium cages personalized for a specific patient using 3D printers. These cages have shown acceptable results as well [(57).]

References:

1. B. CR. Posterior lumbar interbody fusion updated. Clin Orthop Relat Res. 1985;193:16–9.
2. Lin, P. M., Cautilli, R. A., & Joyce MF. Posterior lumbar interbody fusion. Clin Orthop Relat Res. 1983;180:154–68.
3. Zhang D, Gao X, Jiang J, Shen Y, Ding W, Cui H. Safe placement of pedicle screw in lumbar spine with minimum three year follow-up: a case series and technical note. Int Orthop. 2018;42(3):567–73.
4. Mobbs RJ, Phan K, Malham G, Seex K, Rao PJ. Lumbar interbody fusion: techniques, indications and comparison of interbody fusion options including PLIF, TLIF, MI-TLIF, OLIF/ATP, LLIF and ALIF. J spine Surg (Hong Kong). 2015;1(1):2–18.
5. Matgé G. Cervical cage fusion with 5 different implants: 250 Cases. Acta Neurochir (Wien). 2002;144(6):539–50.
6. Faldini C, Chehrassan M, Miscione MT, Acri F, D'Amato M, Pungetti C, et al. Single-level anterior cervical discectomy and interbody fusion using PEEK

anatomical cervical cage and allograft bone. J Orthop Traumatol. 2011;12(4):201–5.
7. Struwe C, Hermann PC, Bornemann R, Plöger M, Roessler PP, Strauss AC, et al. A novel PLIF PEEK interbody cage with an impactionless insertion technology: A case series with a mid-term follow up of three years. Technol Heal Care. 2017;25(5):949–57.
8. El Masry MA, Khayal H, Salah H. Unilateral transforaminal lumbar interbody fusion (TLIF) using a single cage for treatment of low grade lytic spondylolisthesis. Acta Orthop Belg. 2008;74(5):667–71.
9. de Kunder SL, van Kuijk SMJ, Rijkers K, Caelers IJMH, van Hemert WLW, de Bie RA, et al. Transforaminal lumbar interbody fusion (TLIF) versus posterior lumbar interbody fusion (PLIF) in lumbar spondylolisthesis: a systematic review and meta-analysis. Spine J [Internet]. 2017;17(11):1712–21. Available from: https://doi.org/10.1016/j.spinee.2017.06.018
10. Wigfield CC, Nelson RJ. Nonautologous interbody fusion materials in cervical spine surgery: How strong is the evidence to justify their use? Spine (Phila Pa 1976). 2001;26(6):687–94.
11. Rajaee SS, Bae HW, Kanim LEA, Delamarter RB. Spinal fusion in the United States: Analysis of trends from 1998 to 2008. Spine (Phila Pa 1976). 2012;37(1):67–76.
12. Norton RP, Bianco K, Klifto C, Errico TJ, Bendo JA. Degenerative spondylolisthesis: An analysis of the nationwide inpatient sample database. Spine (Phila Pa 1976). 2015;40(15):1219–27.
13. Brunette DM, Tengvall P, Textor M, Thomsen P. Titanium in Medicine [Internet]. Berlin, Heidelberg: Springer Berlin Heidelberg; 2001 [cited 2020 Oct 11]. (Engineering Materials). Available from: http://link.springer.com/10.1007/978-3-642-56486-4
14. Van Noort R. Titanium: The implant material of today [Internet]. Vol. 22, Journal of Materials Science. Kluwer Academic Publishers; 1987 [cited 2020 Oct 11]. p. 3801–11. Available from: https://link.springer.com/article/10.1007/BF01133326
15. Hwang SL, Hwang YF, Lieu AS, Lin CL, Kuo TH, Su YF, et al. Outcome analyses of interbody titanium cage fusion used in the anterior discectomy for cervical degenerative disc disease. J Spinal Disord Tech. 2005;18(4):326–31.
16. Salame K, Ouaknine GER, Razon N, Rochkind S. The use of carbon fiber cages in anterior cervical interbody fusion: report of 100 cases. Neurosurg Focus. 2002;12(1):1–5.
17. Chitnavis B, Barbagallo G, Selway R, Dardis R, Hussain A, Gullan R. Posterior lumbar interbody fusion for revision disc surgery: Review of 50 cases in which carbon fiber cages were implanted. J Neurosurg. 2001;95(2 SUPPL.):190–5.
18. Krätzig T, Mende KC, Mohme M, Kniep H, Dreimann M, Stangenberg M, et al. Carbon fiber–reinforced PEEK versus titanium implants: an in vitro comparison of susceptibility artifacts in CT and MR imaging. Neurosurg Rev. 2020;
19. Kanayama M, Cunningham BW, Haggerty CJ, Abumi K, Kaneda K, McAfee PC. In vitro biomechanical investigation of the stability and stress-shielding effect of lumbar interbody fusion devices. J Neurosurg. 2000;93(2 SUPPL.):259–65.
20. Cho D, Liau W, Lee W, Al ET. Preliminary experience using a polyetheretherketone (PEEK) cage in the treatment of cervical disc disease. Neurosurgery. 2002;51(6):1343–50.
21. Rohe SM, Engelhardt M, Harders A, Schmieder K. Anterior cervical discectomy and titanium cage fusion 7-year follow-up. Zentralbl Neurochir. 2009;70(4):180–6.
22. Sugawara T, Itoh Y, Hirano Y, Higashiyama N, Mizoi K. Long term outcome and adjacent disc degeneration after anterior cervical discectomy and fusion with titanium cylindrical cages. Acta Neurochir (Wien). 2009;151(4):303–9.
23. Liu JT, Chen SY, Su CH, Yang TH. RADIOGRAPHIC OUTCOMES of ANTERIOR CERVICAL DISCECTOMY and FUSION SURGERY by USING CUSHIONED TITANIUM CAGE. J Musculoskelet Res. 2020;23(2):1–7.
24. Lee JH, Jeon DW, Lee SJ, Chang BS, Lee CK. Fusion rates and subsidence of morselized local bone grafted in titanium cages in posterior lumbar interbody fusion using quantitative three-dimensional computed tomography scans. Spine (Phila Pa 1976). 2010;35(15):1460–5.
25. Hahn BD, Park DS, Choi JJ, Ryu J, Yoon WH, Choi JH, et al. Osteoconductive hydroxyapatite coated PEEK for spinal fusion surgery. Appl Surf Sci [Internet]. 2013;283:6–11. Available from: http://dx.doi.org/10.1016/j.apsusc.2013.05.073
26. Han CM, Lee EJ, Kim HE, Koh YH, Kim KN, Ha Y, et al. The electron beam deposition of titanium on polyetheretherketone (PEEK) and the resulting enhanced biological properties. Biomaterials [Internet]. 2010;31(13):3465–70. Available from: http://dx.doi.org/10.1016/j.biomaterials.2009.12.030
27. Hoppe S, Albers CE, Elfiky T, Deml MC, Milavec H, Bigdon SF, et al. First results of a new vacuum plasma sprayed (VPS) titanium-coated carbon/PEEK composite cage for lumbar interbody fusion. J Funct Biomater. 2018;9(1):1–10.
28. Manabe H, Sakai T, Morimoto M, Tezuka F, Yamashita K, Takata Y, et al. Radiological outcomes of posterior lumbar interbody fusion using a titanium-coated PEEK cage. J Med Investig. 2019;66(1.2):119–22.
29. Li P, Jiang W, Yan J, Hu K, Han Z, Wang B, et al. A novel 3D printed cage with microporous structure and in vivo fusion function. J Biomed Mater Res A. 2019;107(7):1386–92.
30. Krafft PR, Osburn B, Vivas AC, Rao G, Alikhani P. Novel titanium cages for minimally invasive lateral lumbar interbody fusion: First assessment of subsidence. Spine Surg Relat Res. 2020;4(2):171–7.
31. Liebsch C, Aleinikov V, Kerimbayev T, Akshulakov S, Kocak T, Vogt M, et al. In vitro comparison of personalized 3D printed versus standard expandable titanium vertebral body replacement implants in the mid-thoracic spine using entire rib cage specimens. Clin Biomech [Internet]. 2020;78(February):105070. Available from: https://doi.org/10.1016/j.clinbiomech.2020.105070
32. Lee DY, Park YJ, Song SY, Jeong ST, Kim DH. Risk factors for posterior cage migration after lumbar

interbody fusion surgery. Asian Spine J. 2018;12(1):59–68.
33. Reid JJ, Johnson JS, Wang JC. Challenges to bone formation in spinal fusion. J Biomech [Internet]. 2011;44(2):213–20. Available from: http://dx.doi.org/10.1016/j.jbiomech.2010.10.021
34. https://www.jnjmedicaldevices.com/.
35. https://www.stryker.com/.
36. https://www.icotec-medical.com/home.html/.
37. https://www.ulrichmedical.de /.
38. https://www.medtronic.com/.
39. https://www.zimmerbiomet.com/.
40. Wrangel C Von, Karakoyun A, Buchholz KM, Süss O, Kombos T, Woitzik J, et al. Fusion Rates of Intervertebral Polyetheretherketone and Titanium Cages without Bone Grafting in Posterior Interbody Lumbar Fusion Surgery for Degenerative Lumbar Instability. J Neurol Surgery, Part A Cent Eur Neurosurg. 2017;78(6):556–60.
41. Hasegawa T, Ushirozako H, Shigeto E, Ohba T, Oba H, Mukaiyama K, 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). 2020;45(15):E892–902.
42. Rickert M, Fleege C, Tarhan T, Schreiner S, Makowski MR, Rauschmann M, et al. Transforaminal lumbar interbody fusion using polyetheretherketone oblique cages with and without a titanium coating. Bone Jt J. 2017;99B(10):1366–72.
43. Chen Y, Wang X, Lu X, Yang L, Yang H, Yuan W, et al. Comparison of titanium and polyetheretherketone (PEEK) cages in the surgical treatment of multilevel cervical spondylotic myelopathy: A prospective, randomized, control study with over 7-year follow-up. Eur Spine J. 2013;22(7):1539–46.
44. Nemoto O, Asazuma T, Yato Y, Imabayashi H, Yasuoka H, Fujikawa A. Comparison of fusion rates following transforaminal lumbar interbody fusion using polyetheretherketone cages or titanium cages with transpedicular instrumentation. Eur Spine J. 2014;23(10):2150–5.
45. Chou YC, Chen DC, Hsieh WA, Chen WF, Yen PS, Harnod T, et al. Efficacy of anterior cervical fusion: Comparison of titanium cages, polyetheretherketone (PEEK) cages and autogenous bone grafts. J Clin Neurosci [Internet]. 2008;15(11):1240–5. Available from: http://dx.doi.org/10.1016/j.jocn.2007.05.016
46. Campbell PG, Cavanaugh DA, Nunley P, Utter PA, Kerr E, Wadhwa R, et al. PEEK versus titanium cages in lateral lumbar interbody fusion: A comparative analysis of subsidence. Neurosurg Focus. 2020;49(3):1–9.
47. Kashii M, Kitaguchi K, Makino T, Kaito T. Comparison in the same intervertebral space between titanium-coated and uncoated PEEK cages in lumbar interbody fusion surgery. J Orthop Sci [Internet]. 2020;25(4):565–70. Available from: https://doi.org/10.1016/j.jos.2019.07.004
48. Christensen FB, Laursen M, Gelineck J, Eiskjær SP, Thomsen K, Bünger CE. Interobserver and Intraobserver Agreement of Radiograph Interpretation With and Without Pedicle Screw Implants. Spine (Phila Pa 1976). 2001;26(5):538–43.
49. Cuzzocrea F, Ivone A, Jannelli E, Fioruzzi A, Ferranti E, Vanelli R, et al. PEEK versus metal cages in posterior lumbar interbody fusion: a clinical and radiological comparative study. Musculoskelet Surg [Internet]. 2019;103(3):237–41. Available from: https://doi.org/10.1007/s12306-018-0580-6
50. Sakaura H, Ohnishi A, Yamagishi A, Ohwada T. Early fusion status after posterior lumbar interbody fusion with cortical bone trajectory screw fixation: A comparison of titanium- coated polyetheretherketone cages and carbon polyetheretherketone cages. Asian Spine J. 2019;13(2):248–53.
51. Vazifehdan F, Karantzoulis VG, Igoumenou VG. Sagittal alignment assessment after short-segment lumbar fusion for degenerative disc disease. Int Orthop. 2019;43(4):891–8.
52. Yang MY, Chang HH, Chao SC. Clinical and radiologic outcomes of two types of cages used in the treatment of degenerative lumbar diseases: Novel titanium cages versus peek cages. J Musculoskelet Res. 2020 Aug 15;
53. Schnake KJ, Fleiter N, Hoffmann C, Pingel A, Scholz M, Langheinrich A, et al. PLIF surgery with titanium-coated PEEK or uncoated PEEK cages: a prospective randomised clinical and radiological study. Eur Spine J [Internet]. 2020;(0123456789). Available from: https://doi.org/10.1007/s00586-020-06642-x
54. Marchi L, Abdala N, Oliveira L, Amaral R, Coutinho E, Pimenta L. Radiographic and clinical evaluation of cage subsidence after stand-alone lateral interbody fusion. J Neurosurg Spine. 2013;19(1):110–8.
55. Kurtz SM, Lau E, Ong KL, Carreon L, Watson H, Albert T, et al. Infection risk for primary and revision instrumented lumbar spine fusion in the Medicare population: Clinical article. J Neurosurg Spine. 2012;17(4):342–7.
56. Saavedra-Pozo FM, Deusdara RAM, Benzel EC. Adjacent segment disease perspective and review of the literature. Ochsner J. 2014;14(1):78–83.
57. Burnard JL, Parr WCH, Choy WJ, Walsh WR, Mobbs RJ. 3D-printed spine surgery implants: a systematic review of the efficacy and clinical safety profile of patient-specific and off-the-shelf devices. Eur Spine J [Internet]. 2020;29(6):1248–60. Available from: https://doi.org/10.1007/s00586-019-06236-2