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Review article

Titanium vs. polyetheretherketone (PEEK) interbody fusion: Meta-analysis and review of the literature

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ABSTRACT

Spinal interbody fusion is a standard and accepted method for spinal fusion. Interbody fusion devices include titanium (Ti) and polyetheretherketone (PEEK) cages with distinct biomechanical properties. Titanium and PEEK cages have been evaluated in the cervical and lumbar spine, with conflicting results in bony fusion and subsidence. Using Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines, we reviewed the available literature evaluating Ti and PEEK cages to assess subsidence and fusion rates. Six studies were included in the analysis, 3 of which were class IV evidence, 2 were class III, and 1 was class II. A total of 410 patients (Ti-228, PEEK-182) and 587 levels (Ti-327, PEEK-260) were studied. Pooled mean age was 50.8 years in the Ti group, and 53.1 years in the PEEK group. Anterior cervical discectomy was performed in 4 studies (395 levels) and transforaminal interbody fusion in 2 studies (192 levels). No statistically significant difference was found between groups with fusion (OR 1.16, 95% C.I 0.59–2.89, p = 0.686, I^2 = 49.7%) but there was a statistically significant the rate of subsidence with titanium (OR 3.59, 95% C.I 1.28–10.07, p = 0.015, I^2 = 56.9%) at last follow-up. Titanium and PEEK cages are associated with a similar rate of fusion, but there is an increased rate of subsidence with titanium cage. Future prospective randomized controlled trials are needed to further evaluate these cages using surgical and patient-reported outcomes.

1. Introduction

It has been estimated that over 400,000 spinal fusions are performed every year in the United States [1,2], of which approximately 150,000 involve the cervical spine and 200,000 involve the lumbar spine. One report noted that, in patients undergoing surgery for degenerative spondylolisthesis, as many as 83% of the procedures involved the use of an interbody cage [3].

Cage technology for spinal fusion was first proposed by Bagby in 1988 [4]. Titanium (Ti) and its alloys had already been used by orthopedic surgeons since the 1940s [5]. Titanium was chosen for its excellent corrosion resistance, low density and its ability to enhance cell adhesion and osseointegration [5,6]. While Ti had favorable fusion rates, a noted shortcoming was subsidence [7–9], or settling into the adjacent vertebral bodies due to the differences in the modulus of elasticity [10]. As a result, polyetheretherketone (PEEK) cages were introduced in the 1990s as an alternative due to their elastic modulus properties. PEEK is a hydrophobic polymer that is biomechanically similar to cortical bone. However, PEEK is chemically inert and does not allow for protein absorption and promotion of cell adhesion and bone contact [11,12]. The characteristics of each cage type are summarized in Table 1.

Several studies have evaluated the role of titanium and PEEK cages in spinal fusion, both in cervical and lumbar spine. Results have not always been consistent in the effect of these materials on fusion rates and settling [7,13,14]. To evaluate the differences of these materials, we conducted a systematic review and a meta-analysis of all available literature looking at the role of Ti and PEEK cages in spinal surgery and associated surgical and radiographic outcomes, including cage subsidence, fusion rates, and patient-reported outcomes (PRO).

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Table 1
Summary of advantages and disadvantages of Titanium and PEEK cages.

Property	Titanium	Polyetheretherketone (PEEK)
Introduction to market	1980s	1990s
Elasticity	Higher	Lower
Radiodensity	Radiopaque	Radiolucent
Modulus	100–110 GPa	3.5 GPa
Promotion of osseointegration	Higher	Lower
Subsidence rates	Higher	Lower
Risk of metal allergy	Yes	No

2. Methods

2.1. Data source and search strategy

We used the guidelines outlined in the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) [15]. The databases queried included Medline/PubMed, Google Scholar, Scopus, and Cochrane; data were collected from published studies from all available years. The keywords used to identify articles of interest included the following Boolean search string: "titanium" AND "polyetheretherketone" or "PEEK" AND "cage" or "interbody" AND "cervical fusion" or "lumbar fusion" or "interbody fusion".

2.2. Eligibility criteria

Studies eligible were those that directly compared Ti and PEEK cages in spinal fusion procedures for a primary diagnosis of degenerative spinal disease, intervertebral disc herniation, ossified posterior longitudinal ligament, or trauma. Moreover, included studies needed to report at least one of the following outcomes: patient-reported outcomes, subsidence, or bone union rates.

Exclusion criteria were: (1) less than 10 patients in each study arm; (2) follow-up of less than 12 months; (3) cage implantation in the setting of intraspinal infection; (4) case reports and letters to the editors; (5) abstracts or poster presentations in conferences, where access to full data report was not available; (6) editorials, reviews, and commentary articles. We also performed a manual search to ensure that no relevant studies were missed. Two independent reviewers examined the results of the electronic search. In cases of discordance, the opinions of the senior authors were counted towards the final decision, and in cases of concern for overlapping cohorts, authors of the studies were contacted directly for clarification, and the study with the most complete reporting was selected.

2.3. Data extraction and processing

The following data was extracted: methodology data, study design, country, type of cage, number of patients, patient demographics and comorbidities, baseline PROs, operative data (number of levels fused, estimated blood loss, procedure type, operative time), postoperative PROs at 12 months and at last follow-up, as well as fusion and subsidence rates. Patient-reported outcomes measures were: Neck Disability Index (NDI); Oswestry Disability Index (ODI); Visual Analog Scale (VAS) for neck, arm, low back or leg; Japanese Orthopedic Association Score; and Odom's Criteria. Reference lists were created, compared, and reviewed for relevance and assessed using the prespecified inclusion and exclusion criteria. When mean and standard deviation of values were not available, estimations were made, if possible, using the reported graphs and published methodologies [16,17]. Data were extracted by the first reviewer, and accuracy of data entry was confirmed by the second reviewer.

2.4. Evidence quality assessment

The quality of evidence for each study was assessed independently by two reviewers using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) protocol [18]. Each study was rated overall as either high, moderate, low, or very low based on study design, limitations, and results.

2.5. Statistical analysis

Independent *t*-tests were used to evaluate for differences between groups, and Chi-square analysis was used for categorical variables. In all cases were assessed, Levene's test was not significant such that equal variances were assumed. Arthrodesis was heterogeneously assessed among studies but was deemed successful using some combination of these parameters: less than 2–3 degrees of movement at the operated segment and no movement of the spinous processes on flexion-extension films; absence of a radiolucent gap between graft and endplate; and/or presence of bridging bony trabeculae at the graft-endplate interface. Subsidence was defined as loss of intervertebral height was 2 or 3 mm, as the studies reviewed were mixed in their definition. Fusion success and subsidence rate defined by radiographic follow-up at 12 months post-operatively was calculated using the odds ratio (OR) as a summary statistic. We calculated the I^2 statistic to estimate the variation in fusion and subsidence rates across the included studies secondary to heterogeneity rather than chance. Values greater than 50% were considered as substantial heterogeneity. In this meta-analysis, the pooled effect size with upper and lower confidence intervals was calculated utilizing a random effects model to account for the possible clinical diversity and methodological variation between the studies. Specific analyses on confounding factors were not possible because the raw data were not available. Analyses were performed in SPSS (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) Forest plots were created using Microsoft Excel, version 14.

3. Results

3.1. Literature search results and study characteristics

Our search strategy yielded 875 studies. After removing 725 duplicate studies and applying inclusion and exclusion criteria to the study's titles and abstracts, 6 articles were finally included in. The flowchart of our electronic search process is summarized in Fig. 1.

All of the included studies were conducted at single institutions; five were retrospective, observational and one was a prospective, randomized trial [Table 2]. Two studies were carried out in Japan [14,19], two in Taiwan [8,9], one in China [7], and one in Germany [13]. A total of 410 patients were analyzed (Ti-228, PEEK-182). The average follow-up time ranged between 12 and 102.1 months, with the pooled mean follow-up period being 36 months (Ti-34 months, PEEK-38 months). Based on the GRADE assessment, the quality of evidence was deemed as very low in 5 of the studies and high in the remaining 1.

3.2. Demographics

Demographics from each study are reported in Table 3. An independent samples *t*-test was conducted to examine whether there was a significant difference between Ti vs. PEEK groups in regards to age. Mean age and standard deviation of the Ti and PEEK groups were 50.8 (7.6) and 53.2 (7.8), respectively. There was no statisti-