Editorial

Editorial on "Transforaminal lumbar interbody fusion using polyetheretherketone oblique cages with and without a titanium coating: a randomised clinical pilot study"

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Comment on: Rickert M, Fleege C, Tarhan T, *et al.* Transforaminal lumbar interbody fusion using polyetheretherketone oblique cages with and without a titanium coating: a randomised clinical pilot study. Bone Joint J 2017;99-B:1366-72.

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In the paper, entitled "Transforaminal lumbar interbody fusion using polyetheretherketone oblique cages with and without a titanium coating: a randomised clinical pilot study", the authors presented data from a randomized pilot study with either polyetheretherketone (PEEK) or titanium coated peek cages (1).

The author's data consist of 40 patients with low back pain for at least 6 months operated with an open transforaminal lumbar interbody fusion (TLIF) technique, due to degenerative disc disease (DDD), spinal stenosis, or spondylolisthesis both degenerative and isthmic.

The type of cage inserted was blinded to the patients. Their primary outcomes were Oswestry Disability Index (ODI), Euroqol-5D (EQ-5D), back and leg pain and fusion rate after 3 and 12 months.

The H1 hypothesis was not defined in the paper, but from their study setup, we suppose that their expectation was the PEEK cage coated with titanium would result in a faster fusion and therefore result in a better ODI score already after 3 months.

The authors should be commended their effort to put up a prospective randomized trial, registered in Clinicaltrails.gov (NCT03063008)

However, their patient groups were to small. The calculations done using the standard deviation (SD) do not seem to be correct for sample size estimation. In the statistical analysis of their paper, a 12.8-point difference in the ODI was adapted from previous publications, however, the SD of their present groups was larger than 12.8.

When evaluating ODI at 3, 6 and 12 months, the variations were big. The authors did not give the SD, but the range of 95% CI which was always larger than 15 points.

The paper does not state whether the data were normally distributed. Supposing the data were normally distributed, SD could be calculated from the 95% CI. For example, at 1-year follow-up, the SD for ODI of PEEK cage is 20.5 which was much higher than minimal clinical important difference (MCID =12.8).

Either the data was not normally distributed or the threshold for MCID of 12.8 was inappropriate for their present setting. In case their data was not normally distributed, which is often the case dealing with ordinal variable; the authors should have used non-parametric tests in order to do a right comparison between their two randomized groups. If they had wanted to detect the difference of 12.8 based on the present big variation (SD 20.5) and their material was normally distributed, the sample size in each group in our calculation is at least 40 patients in each group [equation for estimation $N = 2\sigma^2 \times f(\alpha,\beta)/(\mu_1 - \mu_2)$]. σ represent SD, $\alpha = 0.05$, $\beta = 0.2$, difference of ODI ($\mu_1 - \mu_2$) was adapted from literature 12.8.

So according to their results presented in the article, their calculation does not seem to be appropriate and they

could have gained knowledge of correct sample size taking their own SD by consulting statistical expertise.

Generally, TLIF cages serve two purposes in spinal fusion procedures: (I) biomechanical support of the anterior column; (II) host of bone graft materials to promote bone healing. Besides these two properties which should be provided by the TLIF cage, different materials and designs have been developed such as titanium, tantalum, PEEK, carbon fiber, hydroxyapatite, biodegradable PLLA/PLA with bullet or even 3D print anatomical shapes.

Among all these cage materials, PEEK is the mostly used material due to its radiolucency and an elastic modulus close to that of human bone. However, due to the hydrophobic surface, PEEK is not friendly for bone ongrowth so there will always be a fibrous layer around the cage. To provide better bone integration, coating of the surface of interbody cage has been investigated for many years. We have previous coated our carbon fiber cage with tantalum that achieved excellent results (2). In the present article, PEEK cage was coated with titanium, which was supposed to provide better bone integration and thus better fusion and clinical outcomes. The desired results were not found which was probably due to type 2 error, i.e., false negative. We know that various factors can affect interbody fusion results, such as endplate preparation, bone graft material quality, fixation stability, systemic illness etc. (3-5). In optimal conditions, the fusion will be achieved no matter what kind of cages are used, which makes it difficult for clinical studies to detect the subtle difference, and due to that, the design of the study was not optimal.

Compared to the anterior lumbar interbody fusion (ALIF) procedure, TLIF can achieve pedicle screw fixation and interbody fusion by the posterior approach alone. However, endplate preparation is a bit more challenging in TLIF due to limited vision. The residual cartilage at the endplate or disc tissue could make a bigger influence on the fusion than, that of surface coating. We have previous demonstrated that the disc tissue could actually influence fusion negatively (6). Another small detail is that most surgeons pack the disc space with autograft before insertion of the TLIF cage. This is reasonable, because the amount of bone graft that can be packed into the cage is so small that healing through the cage is seldom seen on a CT scanning. The typical image is 'a locking pseudo arthrosis' (7,8). When autograft bone is packed anterior to the TLIF cage, the fusion rate is much higher. However, in this scenario the cage only functions as a spacer, the larger the footprint the better mechanical support will be and the lesser risk for subsidence. That is why the subtle change of surface coating wouldn't be detected in the present study settings and sample size. The necessity of coating TLIF cage can also be discussed in this circumstance, coating usually create rough surface and give more friction when inserted into the disc space (9), furthermore, coating could result in debris and delamination and due to that local inflammation (10).

The follow-up period was only 12 months, all quality papers agrees that at least 2 years of follow-up should be a minimum, since many studies have shown that even after that time the immediate conclusion might change over time (11-15).

The follow-up rate in the PEEK group was only 75% (15/20) or less, which is actually a big loss after only 1 year in comparison to other randomized controlled trials (RCTs) looking at lumbar fusions (15-17). That could be a big confounder to the conclusion of the paper.

In the present study, the authors had a complication rate as high as 25 % in the titanium PEEK group and at least 16% in the PEEK group. The complications described can be regarded as severe and leaving the patients with harms due to the procedure, such as persistent leg pain and perforation of the right iliac vein with several revision required.

The conclusion the authors draw from the data presented in this study seem to be incorrect and not in accordance with their own findings. Actually, they found a significant difference between groups at 1-year follow-up in favor of PEEK cage regarding leg pain. This might reflect the higher friction in the titanium coated PEEK cage, which could have resulted in adverse effect to the procedure such as violation of the upper nerve root/ganglion causing chronic radiculopathy or radiculitis when inserting the cage (9,10). Therefore, it could have been reasonable to detect whether the significant raise in leg pain was at the ipsilateral side of the cage insertion.

The question, which needed to be asked overall, is whether the interbody fusion is necessary. With complication rate as high as 25% leaving the patients with persistent radiculopathy afterwards, one might argue that their results are contradictory to the introduction of the paper, where the authors states that TLIF is an established, safe technique for fusing the lumbar spine. Also, their conclusions seem to be contradictory to their own results: "*In conclusion, there were favorable results with both PEEK and TiPEEK cages after instrumented lumbar fusion. No negative effects of the coating were observed, since there was a significant difference in favor of only PEEK regarding leg pain at the end*

point of the study."

The study presents huge problems, severe complications, which is associated with the technically higher demanding procedures in comparison to a posterior lateral fusion (18,19).

Since RCT have shown no benefits in ODI scores at 1-, 2- and 9-year follow-up regarding TLIF in comparison to a standard instrumented posterolateral instrumented fusion (PLF) (16,20-22), in patients with simple lumbar degenerative pathologies. The question the authors have asked, should probably not have been asked into this study population with only 1 and 2 level degenerative spinal disorder.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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