Efficacy of Platelet-rich Plasma Impregnation for Unidirectional Porous B-tricalcium Phosphate in Lateral Lumbar Interbody Fusion: Study Protocol for a Randomized Controlled Trial

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Research Article

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Abstract

Background

Platelet-rich plasma has been increasingly used in spinal fusion surgery. However, the efficacy of platelet-rich plasma in lateral lumbar interbody fusion is unclear. In Japan, Affinos® (Kuraray Co., Tokyo, Japan), which is a β-tricalcium phosphate artificial bone, has been increasingly used for spinal fusion as a bone graft. The purpose of this trial is to demonstrate whether Affinos® impregnated with platelet-rich plasma can achieve a higher fusion rate, more rapid fusion, and better clinical outcomes than Affinos® alone.

Methods/Design

The current study is a prospective randomized controlled trial. The current trial will include consecutive patients scheduled for lateral lumbar interbody fusion. Since an intervertebral cage for lateral lumbar interbody fusion has two spaces for a bone graft, two bone grafts are inserted for each intervertebral level. In the current study, an artificial bone with plate-rich plasma will be inserted into one space and an artificial bone without platelet-rich plasma will be inserted into the other space. We will compare the fusion rates between the bone graft with and without platelet-rich plasma. Our primary endpoint will be the interbody fusion rate at 1 year after surgery.

Discussion

The current trial will verify the efficacy of platelet-rich plasma with Affinos® for bony fusion in lateral lumbar interbody fusion. This trial will provide substantial evidence for the effectiveness and safety of platelet-rich plasma in spinal fusion surgery.

Trial registration

Japan Registry of Clinical Trials (jRCT), ID: jRCTb032200199. First registered on 13 November 2020, https://jrct.niph.go.jp/latest-detail/jRCTb032200199. jRCT is approved as a member of the Primary Registry Network of WHO ICTRP.

Background

Spinal fusion is a common surgery performed for spinal degenerative diseases, spinal fractures, and spinal deformities. The use of the lateral lumbar interbody fusion (LLIF) procedure for the treatment of lumbar spinal pathologies is increasing owing to the associated advantages of this procedure [1]. In Japan, artificial bone is mostly used as a graft material for LLIF [2]. Although surgical outcomes associated with spinal fusion have improved due to innovation in spinal instrumentation [3], bony fusion is essential to prevent pseudoarthrosis.

Affinos® (Kuraray Co., Tokyo, Japan) is a β-tricalcium phosphate artificial bone with a porosity of 57% consisting of a novel unidirectional porous structure, in which intercommunicating holes of 25–300 μm

are arranged in one direction [2]. In Japan, Affinos® has been increasingly used for spinal fusion with acceptable results, while the use of an autologous bone as a bone graft is commonly applied in many fields requiring bony fusion [2, 4].

Platelet-rich plasma (PRP) is a blood plasma containing concentrated autologous platelets with several growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), and insulin-like growth factor (IGF) [5, 6, 7]. Therefore, PRP has been used to accelerate bone and soft tissue healing not only in oral dentistry, dermatology, ophthalmology, and sports medicine, but also in spinal fusion surgery [8, 9, 10, 11, 12].

The question remains whether PRP can accelerate bony fusion in LLIF. Additionally, there have been no reports demonstrating the efficacy of PRP combined with β-tricalcium phosphate artificial bone in LLIF.

The purpose of this study is to demonstrate whether Affinos® impregnated with PRP can achieve a higher fusion rate, more rapid fusion, and better clinical outcomes than Affinos® alone.

Methods

Design of the study

The study is a prospective randomized controlled trial study.

Study procedures

The outline of this study is shown in figure 1. Consecutive patients scheduled for LLIF will be enrolled in this trial. The target sample size for this study trial is 15 patients with a total of 40 intervertebral levels. This trial has been approved by the institutional review board of University of Tsukuba hospital, and consent for participation in the trial will be obtained from all patients (jRCTb032200199).

GPS® III (Zimmer Biomet, Warsaw, IN, USA) will be used to prepare a PRP. A total of 52 mL of peripheral blood will be drawn from each patient before the surgery. The withdrawn blood will be centrifuged for 15 min at 3200 rpm. After elimination of platelet-poor plasma, PRP will be obtained by extracting the buffy coat layer.

CoRoent XL PEEK cage® (NuVasive, San Diego, CA, USA) will be used as an intervertebral fusion cage for the LLIF. A block-type Affinos® will be used as a bone graft in the intervertebral cage. Each cage has two spaces for the bone graft; one space will be filled with an artificial bone block impregnated with PRP, and the other will be filled with an artificial bone block without PRP. Therefore, two artificial bone blocks can be grafted at each intervertebral level. The side of the bone graft with PRP will be alternately set in the order of insertion.

Our primary endpoint is the interbody fusion rate at 1 year after surgery. Plain radiographs and computerized tomography (CT) multi-planar reconstruction coronal and sagittal images will be obtained

for the evaluation of interbody fusion at 1 year after the surgery. Interbody fusion will be determined when no instability is identified in flexion-extension radiographs, and bony continuity will be identified on CT images [2].

The secondary endpoints are as follows: (1) the interbody fusion rate at 6 months after surgery; (2) temporal changes in grafted artificial bone such as resorption and remodeling; (3) bony contact between the cage and vertebral endplates; (4) visual analog scale (VAS), Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOA-BPEQ), Oswestry disability index (ODI), and European Quality of Life 5 dimensions (EQ-5D).

Inclusion criteria

The inclusion criteria are as follows: (1) patients who are scheduled for LLIF for a lumbar degenerative disease; (2) patients who are scheduled for LLIF between 1 and 4 intervertebral levels; (3) patients aged >20 years; and (4) patients who agree to participate in the current trial and from whom informed consent has been obtained both orally and in writing.

Exclusion criteria

Exclusion criteria are as follows: (1) patients with a history of lumbar surgery, infectious spondylitis, and spinal tumor; (2) patients administered another trial drug within 3 months before the commencement of this study; (3) patients with comorbidities, such as abnormal bone metabolism and hemodialysis, that cause inferior osteogenic ability; (4) patients with uncontrolled diabetes mellitus; (5) patients with anemia (hemoglobin <9.0 g/dL); (6) patients with hematological disorders; (7) patients who are pregnant or nursing; (8) patients with metallic allergies; and (9) patients who cannot provide a written consent.

Sample size estimation

The target sample size for this study is 15. Since each patient will undergo LLIF between 1 to 4 intervertebral levels, more than 40 intervertebral levels are expected to be included in this study. Therefore, at least 80 bone graft spaces will be included to evaluate bony fusion. A sample size calculation was performed based on the results of previous studies [2, 13]. In the previous study, the fusion rate of LLIF with Affinos® was 70.9%. In contrast, the intervertebral fusion rate with autologous iliac crest bone was 94.5%. Based on these parameters, we calculated a sample size of 40 bone graft spaces per group with a power of 80% and an alpha of 5% (two-tailed).

Statistical Analyses

For the baseline characteristics, summary statistics will comprise frequencies and proportions for categorical variables and means and standard deviations for continuous variables. Patient characteristics will be compared using a χ^2 test for categorical variables and a t-test or Mann-Whitney U test for continuous variables.

The intervertebral fusion rate in each cage space will be calculated for primary endpoint analysis. A χ^2 test will be performed to compare the fusion rates between bone grafts with and without PRP.

For the secondary endpoint analysis, a χ^2 test will be performed to compare the fusion rates between bone grafts with and without PRP at 6 months. Multivariate analyses will be performed to assess the relationship of bony fusion with VAS, JOA-BPEQ, ODI, and EQ-5D scores.

Statistical analyses will be performed using SPSS Statistics version 27.0 (International Business Machines Corporation, NY, USA). All p values will be two-sided, and $p < 0.05$ will be considered significant.

Ethics

This trial was approved by the regional ethical review board. The trial will be conducted in accordance with the principles of the World Medical Association (WMA) Declaration of Helsinki.

Patient informed consent

All patients will be given written explanatory materials and consent forms. The principal investigator will provide patients with sufficient information before obtaining informed consent.

Public disclosure and publication policy

The outline of the trial is registered on the public registration site, Japan Registry of Clinical Trials (jRCT), prior to the implementation of the trial. jRCT is approved as a member of the Primary Registry Network of WHO ICTRP. The results of the trial will be published in an English journal after the final registration is completed on jRCT site.

Discussion

The current study is a confirmative trial to elucidate the efficacy of PRP with Affinos® for bony fusion in LLIF. If this study demonstrates the efficacy of PRP, Affinos® impregnated with PRP could be an alternative for autologous bone grafts with no risk of complications as opposed to that observed with autologous bone harvest. The current study is important to develop a viable procedure for substantial and safe bony fusion in LLIF.

Trial status

This trial is currently being conducted. Recruitment of study patients commenced on February 24, 2021.

Abbreviations

PRP, platelet-rich plasma; LLIF, lateral lumbar interbody fusion; CT: computerized tomography; PDGF, platelet-derived growth factor; TGF-β, transforming growth factor-β; IGF, insulin-like growth factor; VAS, visual analog scale; JOA-BPEQ, Japanese Orthopedic Association Back Pain Evaluation Questionnaire;

ODI: Oswestry disability index; EQ-5D: European quality of life 5 dimensions; jRCT: Japan Registry of Clinical Trials

Declarations

Ethical approval and consent to participate

This trial has been approved by the institutional review board of our hospital, and consent for participation in the trial will be obtained from all patients (jRCTb032200199).

Consent for publication

Consent for publication will be obtained from every participant in this trial.

Availability of data and materials

The datasets are available on the on the public registration site (jRCT).

Competing interests

The authors declare that they have no competing interests.

Funding

This study is being funded by internal resources; therefore, there is no conflict of interest.

Authors' contributions

All authors contributed to the study design. TF, HN, and MY were responsible for the initial conception of the trial. KS, TF, HN, NK, and MY drafted the manuscript. All authors read and approved the final manuscript.

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Not applicable

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Figures

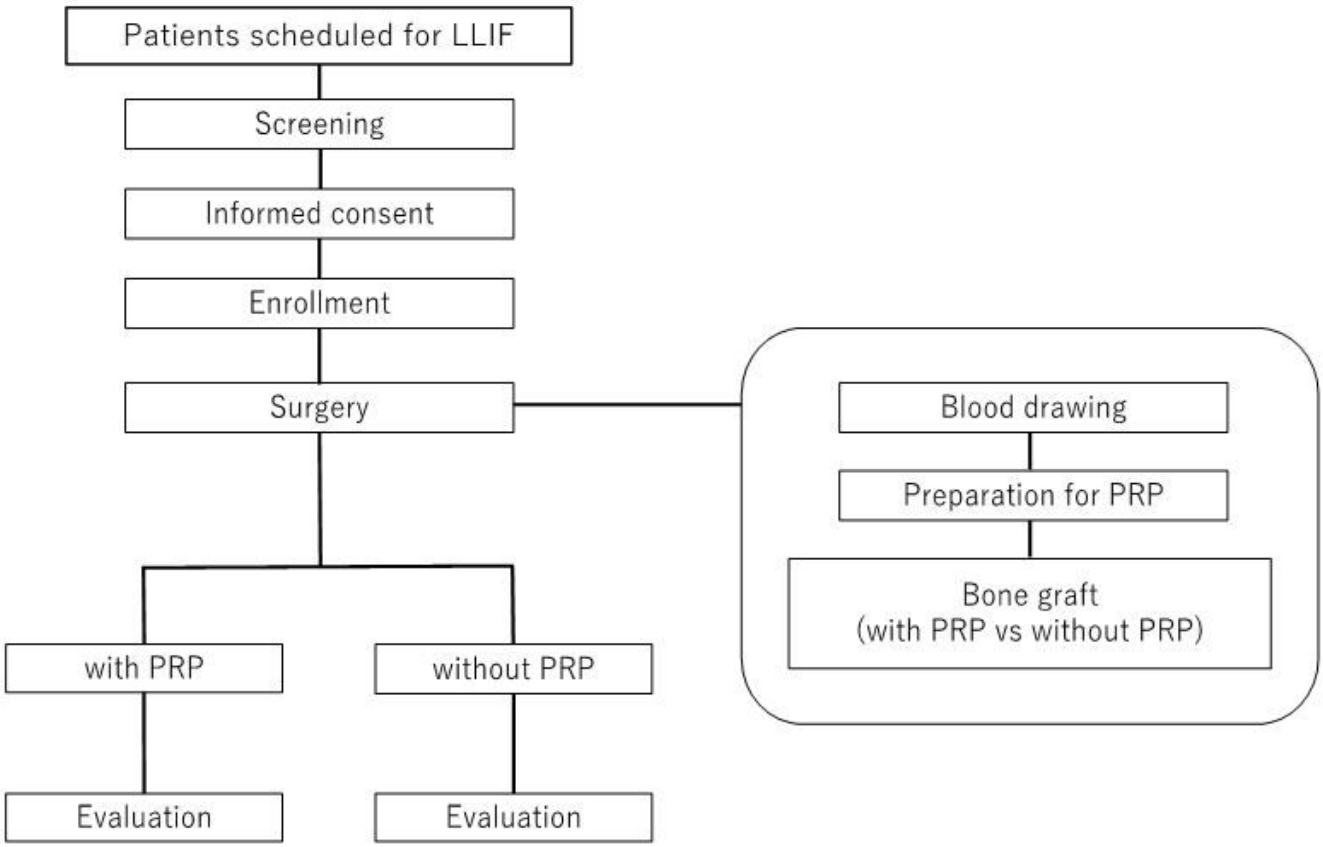

Figure 1

Schematic diagram showing the trial timeline.

Consecutive patients scheduled for lateral lumbar interbody fusion will be recruited for this study. Whole blood will be drawn from each patient to prepare platelet-rich plasma. In an intervertebral cage, one space will be filled with a bone graft impregnated with platelet-rich plasma, and the other will be filled with a bone graft without PRP.