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Combined use of beta-tricalcium phosphate with different porosities can accelerate bone remodelling in open-wedge high tibial osteotomy

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A B S T R A C T

Background/Objective: Beta-tricalcium phosphate (β-TCP) is often used as a gap filler in open-wedge high tibial osteotomy (OWHTO). The aim of the present study was to investigate the effects of using β-TCP with different porosities on bone remodelling after OWHTO.Methods: We evaluated 29 knees in 26 patients that underwent OWHTO using β-TCP with porosities of 60% and 75% (combined group). A further 30 knees in 28 patients that underwent OWHTO using β-TCP with 60% porosity alone were allocated as a control group. In the combined group, a β-TCP block with 75% porosity was inserted into the gap at the cancellous bone site and a β-TCP block with 60% porosity was inserted into the medial cortical bone side. In the control group, a β-TCP block with 60% porosity was inserted into the osteotomy gap. The bone remodelling phases of the inserted β-TCP blocks were evaluated on standard anteroposterior radiographs using the modified van Hemert classification at 3 and 6 months post-operatively.

Results: The rate of satisfactory bone remodelling at the cancellous bone sites was 86.2% (25/29) in the combined group and 0% (0/30) in the control group at 3 months post-operatively ($p<0.05$), progressing to 96.6% (28/29) in the combined group and 20% (6/30) in the control group at 6 months post-operatively ($p<0.05$).

Conclusion: The present study demonstrated that combined use of β-TCP with high and low porosities can significantly enhance bone formation. The combined use of artificial bones with different porosities is useful for early bone remodelling in OWHTO.

1. Introduction

Medial open-wedge high tibial osteotomy (OWHTO) is a well-established surgical procedure for patients with osteoarthritis at a comparatively early stage and osteonecrosis of the medial femoral condyle. In OWHTO, a gap arises at the osteotomy site and its size is dependent on the correction angle. Various methods have been used to address this osteotomy gap in OWHTO, including autogenous bone grafting, allogeneic bone grafting, artificial bone grafting, and no grafting. Bode et al.[1] reported that OWHTO with a locking plate only and no gap fillers provided satisfactory clinical results. In a systematic review, autogenous bone grafting with iliac bone was advantageous for bone union.[2,3] However, iliac bone harvesting involves donor site issues, including pain, bleeding, and additional skin incisions. Although allogeneic bone grafts can also be used, they have disadvantages compared with autogenous bone grafts with regard to bone healing and risk of infection. For these reasons, it is common to use a filling material such as artificial bone for the osteotomy gap. In Asia, soft tissues, including the pes anserinus, are often repaired to create a septum between the implant and the artificial bone to prevent infection. Artificial bone grafts allow retention of the opening gap, through which soft tissue can be repaired.

Several types of artificial bone, including beta-tricalcium phosphate (β-TCP) and hydroxyapatite, have been developed. β-TCP is an

Abbreviations: OWHTO, Medial open-wedge high tibial osteotomy; β-TCP, beta-tricalcium phosphate.

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excellent material that is absorbed to form new bone. Therefore, β-TCP is often used as a gap filler in OWHTO. Various companies have manufactured β-TCP products. Among them, we use Osferion made by Olympus Biomaterials (Tokyo, Japan). There are two types of Osferion associated with high porosity of 75% (Osferion 75%) and low porosity of 60% (Osferion 60%). A difference in β-TCP porosity was reported to influence its mechanical durability and the period before artificial bone blocks are replaced with native bone tissue.[4–6]

Takeuchi et al.[7] reported that the stress concentration at the plate and lateral cortical hinge was reduced by inserting a β-TCP block with 60% porosity into the osteotomy gap, compared with methods that leave the gap open. Therefore, β-TCP with 60% porosity is generally used as a gap filler in OWHTO. However, we have sometimes experienced cases in which β-TCP blocks with 60% porosity were not replaced with bone for a long time and lucent lines appeared around the blocks during that period.

We hypothesized that β-TCP blocks with 75% porosity are superior to those with 60% porosity for block replacement with bone tissue, although 75% porosity is considered to have inferior mechanical strength.

Since 2016, we have used β-TCP blocks with 60% porosity or 75% porosity in the same osteotomy gap. Specifically, a 75% β-TCP block is inserted into the cancellous bone side and a 60% β-TCP block is inserted into the medial cortical bone side to maintain strength. The purpose of this study was to investigate the effects of using β-TCP blocks with different porosities to fill the gap arising during OWHTO.

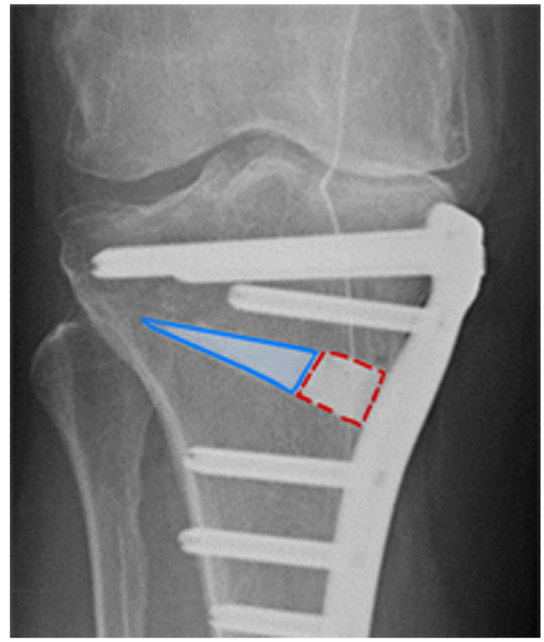

Fig. 1. Typical radiographs in the combined group. A β-TCP block with 75% porosity (dashed line) was inserted into the gap at the cancellous bone site, and an approximately 1-cm long β-TCP block with 60% porosity (solid line) was inserted into the medial cortical bone side. β-TCP: beta-tricalcium phosphate.

2. Materials and methods

For this study, we evaluated 55 knees in 47 consecutive patients who underwent OWHTO using a combination of β-TCP blocks with porosities of 60% and 75% between April 2017 and May 2019. All surgeries were performed by a single surgeon. Among the 55 knees, 25 with incomplete radiographic follow-up data and one with an opening angle $\geq 15^\circ$ were excluded. Finally, 29 knees in 26 patients were investigated retrospectively (combined group) (Table 1). The patients comprised 10 men with 10 treated knees and 16 women with 19 treated knees. The mean age at surgery was 69.2 ± 7.5 years. A further 30 knees in 28 consecutive patients who underwent OWHTO using β-TCP blocks with 60% porosity alone between February 2015 and March 2017 were enrolled as a non-combined group (Table 1). The exclusion criteria for the non-combined group were cases with an opening angle $\geq 15^\circ$ and type 2 hinge fracture by Takeuchi classification.[8] The patients in the non-combined group comprised 10 men with 11 treated knees and 18 women with 19 treated knees, and their mean age at surgery was 64.9 ± 8.5 years.

2.1. Surgical procedure

Knee arthroscopy was performed in all patients to evaluate the extent of cartilage degeneration. The lateral compartment was confirmed to be almost normal in all knees. Assessment of the medial compartment was based on the condition of the medial meniscus and cartilage, and debridement was performed according to the degree of degeneration and damage. A standard bi-plane OWHTO was performed for all cases.[9] The superficial medial collateral ligament and pes anserinus were dissected from the medial cortex of the tibia, and an osteotomy was performed. Lower limb alignment was confirmed under an image intensifier during the operation. The method of artificial bone insertion in the combined group was as follows. A β-TCP block with 75% porosity (Osferion 75%; Olympus Biomaterials) was inserted into the gap at the cancellous bone side and an approximately 1-cm long β-TCP block with 60% porosity (Osferion 60%; Olympus Biomaterials) was inserted into the medial and posteromedial cortical bone side (Fig. 1). A Toris locking plate (Olympus Biomaterials) was used for all cases in the combined group. In the non-combined group, a β-TCP block with 60% porosity was inserted into the osteotomy gap. In the non-combined group, A TomoFix locking plate (Synthes, Paoli, PA, USA) and a Toris locking plate were used in 15 cases each.

All patients were treated in accordance with the following rehabilitation protocol. Mobility training with continuous passive motion was started on postoperative day 3. A 1/2 load was started on postoperative day 21, and thereafter, the weight was increased by 1/3 every week.

Table 1
Background characteristics of the patients in the two groups.

Patient Background	Combined group(n = 29)	Non-combined group(n = 30)	p value
Age(years)	69.2(±7.5)	64.9(±8.5)	0.07
Male/female(patients)	10/19	19/11	0.861
BMI(kg/m^3)	24.9(±2.5)	25.2(±4.0)	0.767
Smoking/non-smoking	9/20	10/20	0.85
Diabetes/non-diabetes	6/23	5/25	0.692
Opening angle(°)	9.86(±2.3)	10.4(±2.5)	0.291

BMI: body mass index.

2.2. Evaluation of bone union

The bone remodelling phases of the artificial bone substitute were evaluated on standard anteroposterior radiographs of the knee for the cancellous and cortical bone sites at 3 and 6 months post-operatively. Evaluation of the cancellous bone site was performed at the centre of the tibial axis. As shown in Fig. 2, the degree of bone formation was divided into four grades using the modified van Hemert classification[10,11]: phase 1, clear distinction between β-TCP and bone; phase 2, unclear distinction between bone and artificial bone, but β-TCP still clearly visible; phase 3, distinction between β-TCP and bone not visible, but β-TCP slightly visible; and phase 4, full bone re-formation, with β-TCP almost invisible. We defined phase 3 or 4 as satisfactory bone formation. This evaluation was performed by two evaluators: SS and TK.

2.3. Statistical analysis

The Mann–Whitney *U* test was used to compare the medians of continuous variables and the chi-square test was used to compare the proportions of categorical variables between the two groups. The level of significance was set at $P < 0.05$. All statistical analyses were conducted using IBM SPSS version 2.23 software (IBM Corp., Armonk, NY, USA). We performed a power analysis (post hoc) on the results of the bone remodelling at the cancellous bone site at 3 and 6 months post-operatively (3 months: effect size 2.47 and alpha 0.05; 6 months: effect size 4.10 and alpha 0.05) between the two groups. In both cases, the power was 1.00. Moreover, we conducted a weighted kappa statistical analysis as an interobserver reliability test.

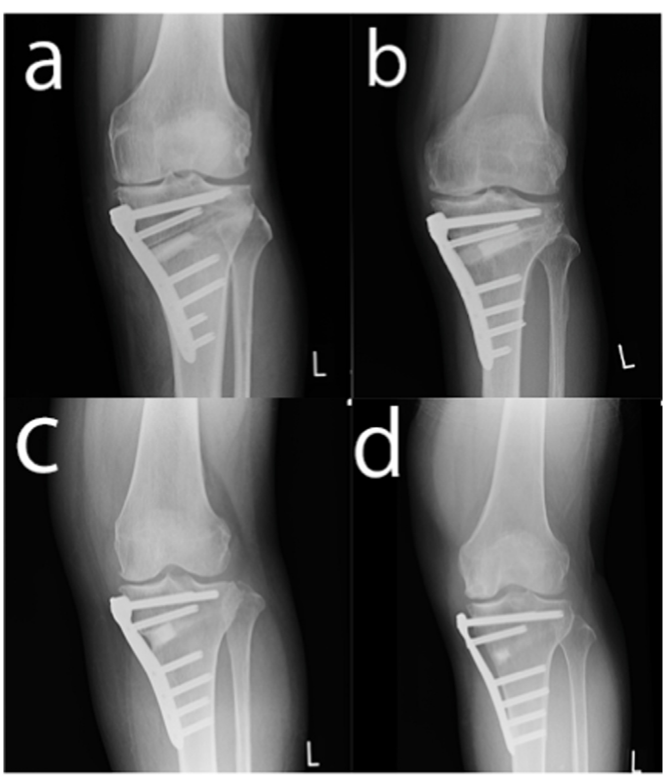

Fig. 2. Typical radiographic images of the bone remodelling phases. **a** Phase 1: clear distinction between β-TCP and bone. **b** Phase 2: unclear distinction between bone and artificial bone, but β-TCP is still clearly visible. **c** Phase 3: distinction between β-TCP and bone not visible, but β-TCP is slightly visible. **d** Phase 4: full bone re-formation, with β-TCP almost invisible. β-TCP: beta-tricalcium phosphate.

2.4. Statement of ethics

The study was approved by the Institutional Review Board at the authors' institution (approval number, 19-9-05). For this type of study, formal consent was not required.

3. Results

On the basis of radiographic evaluations using the modified van Hemert classification, the rate of phase 3 or 4 bone remodelling at the cancellous bone sites was 86.2% (25/29) in the combined group and 0% (0/30) in the non-combined group at 3 months post-operatively, progressing to 96.6% (28/29) in the combined group and 20% (6/30) in the non-combined group at 6 months post-operatively (Table 2). The rate of phase 3 or 4 bone remodelling at the cancellous bone sites in the combined group was significantly higher than that in the non-combined group at 3 and 6 months post-operatively.

At the cortical bone sites, the rate of phase 3 or 4 bone remodelling was 17.2% (5/29) in the combined group and 0% (0/30) in the non-combined group at 3 months post-operatively, progressing to 51.7% (15/29) in the combined group and 16.7% (5/30) in the non-combined group at 6 months post-operatively (Table 3). The rate of phase 3 or 4 bone remodelling at the cortical bone sites in the combined group was significantly higher than that in the non-combined group at 3 and 6 months post-operatively.

No significant difference in operative time was found between the combined group (89.6 ± 8.8 min) and non-combined group (90.7 ± 7.9 min). Correction loss and breakage of inserted β-TCP, and unstable hinge fracture were not observed in either group. The results of the weighted kappa statistic showed a high degree of agreement at 0.82.

4. Discussion

The most important finding of the present study is that the use of β-TCP with 75% porosity allowed earlier replacement with native bone tissue after OWHTO than β-TCP with 60% porosity.

We found that the cases in the combined group exhibited significantly earlier progression of bone formation in the cancellous bone sites compared with those in the non-combined group at 3 and 6 months after OWHTO. Interestingly, a similar tendency was observed at the medial cortex bone sites in the combined and the non-combined groups, even though β-TCP with the same porosity was used at these sites in both groups.

In previous studies, OWHTO without gap filling materials produced good results.[1,12–16] Ferner et al.[12] demonstrated a higher rate of non-union in a group with granular β-TCP compared with a group without implantation. Furthermore, they did not recommend transplantation when the opening gap was less than 10°. Goshima et al.[16] reported that optimal strain energy to achieve a good mechanical environment for gap filling was obtained by strong fixation with a locking plate only and no gap filling materials.

Alternatively, other authors have described the benefits of artificial bone grafting. Takeuchi et al.[7] compared cases with anteromedial and medial tibial plates with and without β-TCP in a mechanical test study using bone models. They demonstrated that an anteromedial plate without β-TCP increased the posterior tilt and induced a greater stress concentration at the osteotomy site. Artificial bone materials distributed the stress concentration around the osteotomy gap and prevented an increase in posterior tilt regardless of the plate positions. In addition, Siboni et al.[17] reported that bone grafting or artificial bone insertion may be considered as a gap filler for patients with an opening angle >10°,

Table 2
Degrees of bone formation at the cancellous bone site.

Modified van Hemert score	Combined group(n = 29)	Non-combined group(n = 30)	p value
3 months post-operatively			
Phase1	0	14	
Phase2	4	16	
Phase3	25	0	
Phase4	0	0	
>Phase3	25	0	<0.001
6 months post-operatively			
Phase1	0	5	
Phase2	1	19	
Phase3	15	6	
Phase4	13	0	
>Phase3	28	6	<0.001

Table 3
Degrees of bone formation at the cortical bone site.

Modified van Hemert score	Combined group(n = 29)	Non-combined group(n = 30)	p value
3 months post-operatively			
Phase1	6	17	
Phase2	18	13	
Phase3	5	0	
Phase4	0	0	
>Phase3	5	0	0.024
6 months post-operatively			
Phase1	3	6	
Phase2	11	19	
Phase3	15	5	
Phase4	0	0	
>Phase3	15	5	0.004

obesity, or an intraoperative lateral hinge fracture. We used 60% β-TCP for cortical bone sites with reference to these reports.

Regarding the effects of differences in β-TCP porosity on bone formation, Knabe et al.[4] reported that β-TCP blocks with high porosity were advantageous for the induction of early bone formation. Tanaka et al.[5] performed OWHTO using β-TCP blocks with porosities of 60% and 75% and investigated the bone formation at the osteotomy site by computed tomography. They observed that β-TCP with 75% porosity was completely resorbed, whereas β-TCP with 60% porosity had approximately one-third remaining at the osteotomy site even at 6 years post-operatively. These findings suggested that β-TCP with 75% porosity is more useful for early bone formation than β-TCP with 60% porosity. However, they used 60% β-TCP for cortical bone and 75% β-TCP for cancellous bone, and did not examine bone union under the same conditions. However, because we compared the degree of bone union of 60% and 75% β-TCP in the same cancellous bone area, we think this more accurately reflects the differences in bone union resulting from differences in porosity.

The cases in the combined group also exhibited the earlier progression of bone formation at the medial cortical bone sites than the cases in the non-combined group, even though the patient characteristics and opening angles in the two groups were similar. This may arise because, in the combined group, the early stabilization of the hinge area achieved by the early bone healing accelerated bone union at the cortical bone side. It is also likely that histological differences might affect bone formation. In previous histological studies, osteoclast-like cells were observed on the surface of the inserted β-TCP at an early stage.[4,18] Furthermore, a lining of osteoblasts was observed on the new bone and active new bone formation was visible. It was reported that the appearance time and number of osteoclast-like cells may differ depending on the difference in porosity.[19,20] Therefore, the use of β-TCP with high porosity may have increased the number of osteoclast-like cells and accelerated the osteogenic cycle even at the medial cortical bone sites. Histological evaluations are absolutely required in future studies to confirm these hypotheses.

The strength of artificial bone decreases as its porosity increases. In previous studies, the mean compressive strengths of β-TCP blocks with porosities of 60% and 75% were 20 MPa and 3 MPa, respectively.[5,6] Thus, the compressive strength of β-TCP with 75% porosity was approximately one-seventh that of β-TCP with 60% porosity. Therefore, we used β-TCP blocks with 60% porosity to fill the medial part of the gap involving the cortical bone where a greater load was applied, and used β-TCP with 75% porosity to fill the lateral part of the gap. As a result, the collapse of the artificial bone and loss of correction were not observed in the combined group during the follow-up period.

In this study, the mean patient age was 69.2 ± 7.5 years in the combined group and 64.9 ± 8.5 years in the non-combined group, and thus somewhat older than indicated for OWHTO. However, Goto et al.[21] reported favourable post-operative results for OWHTO regardless of age. Furthermore, in Asia, OWHTO is often performed on elderly patients because of their active lifestyles.

The limitations of the present study were the small number of cases, the lack of comparison with groups other than the 60% β-TCP alone group, the low rate of follow-up, image evaluation by radiographs only, the use of different plates between the two groups, the lack of objective clinical findings and details of rehabilitation progress, and lack of randomization. We consider computed tomography would be beneficial for the evaluation of medial cortical bone union.

5. Conclusions

The present study showed that the use of β-TCP with 75% porosity allowed earlier replacement with native bone tissue after OWHTO than β-TCP with 60% porosity. A combination of artificial bones with different porosities was useful for obtaining early bone formation while maintaining strength in OWHTO.

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Declaration of competing interest

A conflict of interest occurs when an individual's objectivity is potentially compromised by a desire for financial gain, prominence, professional advancement or a successful outcome. *AP-SMART* Editors strive to ensure that what is published in the Journal is as balanced, objective and evidence-based as possible. Since it can be difficult to distin-guish between an actual conflict of interest and a perceived conflict of interest, the Journal requires authors to disclose all and any potential conflicts of interest.

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