

Special Article - Orthopedic Surgery

Is Injectable Beta-Tricalcium Phosphate Effective as Gap Filler for Medial Open Wedge High Tibial Osteotomy?

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***Corresponding author:** Jae-Hwa Kim, Department of Orthopaedic Surgery, CHA University, Republic of Korea**Received:** August 09, 2016; **Accepted:** September 28, 2016; **Published:** October 03, 2016**Abstract**

We aimed to evaluate whether using novel injectable gel-type beta Tricalcium Phosphate (β -TCP) as gap filler for Medial Open Wedge High Tibial Osteotomy (MOWHTO) is effective. Consecutive 28 patients who were scheduled to undergo biplanar MOWHTO for medial compartmental osteoarthritis were prospectively enrolled. The osteotomy was fixed by an anatomical locking plate and the gap was filled with novel injectable β -TCP. The degree of bone union and maturation of β -TCP was assessed by radiographs and Computed Tomography (CT) scans at postoperative 3 and 12 months. The mechanical Femoro-Tibial Angle (mFTA) was measured and compared between pre and postoperative period. Clinical outcome was evaluated by determining International Knee Documentation Committee (IKDC), Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Scales (VAS) for pain scores. Twenty-five patients (89.3%) were analyzed and all cases showed bony union of osteotomy site without any complication. Serial progress of bone union was found on radiographs and the mean ratio (β -TCP/host bone) of CT attenuation values significantly changed from postoperative 3 months (12.26) to 12 months (8.37) ($P=0.012$), which indicates maturation of β -TCP. The average mFTA significantly changed from preoperative (4.1° varus) to 3 months (4.8° valgus) and maintained at 12 months (4.3° valgus) ($P<0.001$). Significant improvements of the IKDC, WOMAC and VAS pain scores were also seen ($P<0.001$, $P=0.002$ and $P=0.002$ respectively). We found satisfactory bone union and clinical outcome without any complication after using injectable β -TCP as gap filler for MOWHTO.

Keywords: High tibial osteotomy; Beta-tricalcium phosphate; Computed tomography**Introduction**

High tibial osteotomy is an established procedure for the treatment of patients with varus medial compartmental osteoarthritis of the knee, particularly in young and/or active individuals [1]. Two osteotomies; lateral closed wedge and medial open wedge; are possible surgical options. Compared to lateral closed wedge osteotomy, Medial Open Wedge High Tibial Osteotomy (MOWHTO) has advantages including relatively easier performing, preservation of bone stock, correction of the deformity close to its origin, avoidance of fibular osteotomy and predictable and adjustable correction [2]. However, previous studies concerned about risk of nonunion, early collapse or loss of correction after MOWHTO and suggested that some type of osteotomy gap filler is needed [3,4]. Using bone substitutes as gap filler for MOWHTO has been tried to avoid some pitfalls of using autogenous or allogenic bone graft [5,6]. Beta Tricalcium Phosphate (β -TCP) is well known for high biocompatibility and osteoconductivity and rigid wedge or granule type of β -TCP has been used as a bone substitute graft for MOWHTO [7-9]. In this study, we tried to evaluate the radiographic and clinical outcome of MOWHTO using novel injectable β -TCP; which consisted of 100% β -TCP and thermo sensitive hydrogel to provide injectability; as gap filler. Our hypothesis was that MOWHTO using injectable β -TCP as gap filler would result in satisfactory bone union and clinical outcome at 12 months after the surgery.

Materials and Methods

This prospective cohort series was performed according to the declaration of Helsinki for medical research involving human subjects and was organized and approved by the institutional review board of our hospital (protocol number: BD2013-014M). Consecutive patients who were scheduled to undergo MOWHTO were assessed for eligibility. Patients who had grade 3 or 4 Kellgren & Lawrence osteoarthritic changes on lateral or patellofemoral compartment of knee joint, who had valgus or less than 2° of varus limb alignment, who had more than 10° of flexion contracture or less than 90° of knee range of motion or who refused to participate were excluded from the study. We also excluded patients with heavy cigarette smoking, Body Mass Index (BMI) higher than 35 kg/m^2 and exogenous steroid use.

Preoperative evaluation

Full-length double-limb standing anteroposterior radiographs, including the femoral head and ankle, were taken according to the standardized technique described by McGrory, et al. [10]. Mechanical Femoro-Tibial Angle (mFTA) was measured and amount of osteotomy to achieve target correction angle; 5° valgus of mFTA; was decided.

Surgical procedures

All surgical procedures were carried out by a single surgeon

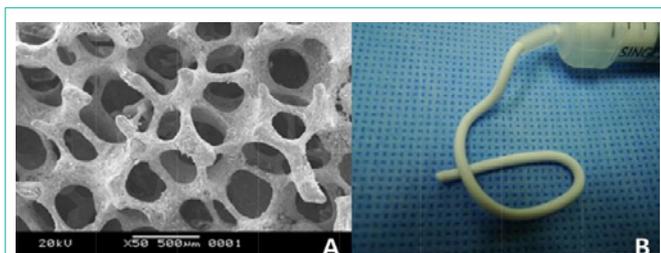


Figure 1: (A) Scanning electron microscope image showing β -TCP granule with 100 to 300 μm pore size. (B) β -TCP is pre-filled in a syringe and ready for injection. The pictures are reproduced by courtesy of the manufacturer.

(JHK). The patient was placed in the supine position with spinal or epidural anesthesia and a thigh tourniquet was inflated during the surgery. Knee arthroscopy was performed first during which the menisci, ligaments and articular cartilage were inspected and concomitant arthroscopic procedures including partial meniscectomy or microfracture were carried out if necessary. Biplanar medial open-wedge HTO was performed according to the method that previously reported under fluoroscopic control [11]. Osteotomy was performed using osteotomes and a calibrated distractor was used to open the osteotomy site in order to achieve the target mFTA; 5° valgus of mFTA; that preoperatively planned. Fixation of osteotomy was performed using an anatomical locking plate (OhtoFix; Ohtomedical Co. Ltd., Goyang, Korea). After plate fixation, 5 cc of β -TCP (EXCELOS inject; CG Bio, Seongnam, Korea) ($\text{Ca}_3(\text{PO}_4)_2$) was injected into the osteotomy gap.

Characteristics of injectable β -TCP

The injectable gel-type β -TCP used in this study is pre-filled in a syringe and consisted of 100% β -TCP granules with 75% porosity and 100 to 300 μm pore size mixed with bio-degradable hydrogel. The hydrogel is highly concentrated polyoxyethylene-polyoxypropylene block co-polymer (Pluronic F127), which ensures the injectability of β -TCP and make the sol-gel transition at 25 °C [12] (Figure 1).

Postoperative managements

Patients were encouraged to start passive range of knee motion and active quadriceps strengthening exercises the day after surgery with hinged knee brace protection. Partial weight bearing with crutches and brace was maintained for 4 weeks and after which full weight bearing was allowed as tolerated.

Postoperative radiographic evaluation

Postoperative mFTA was determined using full-length double-limb standing anteroposterior radiographs taken at 3 and 12 months after surgery. The degree of bone union and maturation of β -TCP was evaluated from knee standing anteroposterior radiographs using the modified van Hemert's grade [13]. This rating represents grade 1 as a vascular phase with clear distinction between the β -TCP and bone; grade 2 as a calcification phase with blurred distinction; grade 3 as an osteoblastic phase with slightly visible distinction; grade 4 as a consolidation phase with no lucent signs despite recognizable osteotomy; and grade 5 as full reformation with no sign of osteotomy. We regarded grades 4 and 5 as bone union, which show no visible line between osteotomy and host bone. Computed Tomography (CT) scans at 3 and 12 months after surgery were taken in order to evaluate serial change of β -TCP resorption and bony union progression.

Table 1: Interobserver reliabilities for radiographic measurements.

Measurement	ICC
Peroperative mFTA	0.78
Postoperative 3 months mFTA	0.72
Postoperative 12 months mFTA	0.79
Modified van Hemert's grade at postoperative 3 month	0.63
Modified van Hemert's grade at postoperative 12 month	0.70
CT attenuation value ratio (β -TCP/host cancellous bone) at 3 month	0.75
CT attenuation value ratio (β -TCP/host cancellous bone) at 12 month	0.76

ICC: Intraclass Correlation Coefficient.

According to the method reported by Tanaka, et al. [8], a CT image of osteotomy level was chosen and divided into areas of injected β -TCP and host bone. The CT attenuation values (in Hounsfield Units: HU) of each area were analyzed. Two investigators (BHK and WK) who were blinded to the study design independently evaluated all plain radiographic and CT measurements using PACS (Picture Archiving and Communication System, Marosis, Infiniti, Seoul and Republic of Korea) and inter-observer reliability for each parameter was calculated.

Clinical evaluation

All patients were evaluated clinically before surgery and 12 months after surgery by using the International Knee Documentation Committee (IKDC) clinical evaluation form and the Western Ontario and McMaster Universities Arthritis Index (WOMAC). In addition, the Visual Analogue Scale (VAS) for pain was recorded.

Statistical analysis

All continuous variables were tested for normality using the Kolmogorov-Smirnov test. We found interobserver reliability using intraclass correlation coefficient values ranging from 0.63 to 0.79 (Table 1). The difference of mFTA between 3 months and 12 months after surgery was determined using paired t-test. Change of the modified van Hemert's grade and the CT attenuation values measured from postoperative 3 and 12 months CT scans were compared using paired t-test. Also, the changes between preoperative and postoperative clinical scores including IKDC, WOMAC and VAS for pain were compared using paired t-test. A p-value < 0.05 was considered statistically significant. The statistical software MedCalc® (Version 11.6; MedCalc Software, Mariakerke, Belgium) and R (ver. 2.12; Comprehensive R Archive Network, Boston, MA, USA) were used for all statistical analysis.

Results

A total of 34 patients were assessed for eligibility and 6 patients who did not meet the inclusion criteria were excluded. Total 28 patients were initially enrolled in this study; however, 3 patients (10.7%) did not take either postoperative 3 or 12 month-CT scan. Therefore, 25 patients (21 women and 4 men) were included in the final analysis. The average age of the patients was 58 years old (range 49 to 67 years old) and average BMI was 25.8 (range 21.9 to 31.1). During the follow-up period, there was no perioperative complication including infection or delayed union.

Bone union and maturation of β -TCP evaluated by the modified Van Hemert's grade showed progression from postoperative 3

Table 2: Progression of bone union and maturation of β -TCP between postoperative 3 and 12 months evaluated using the modified van Hemert's grade.

Grade	3 month	12 month
1	16% (n=4)	
2	52% (n=13)	
3	20% (n=5)	12% (n=3)
4	12% (n=3)	36% (n=9)
5		52% (n=13)

Table 3: Change of the CT attenuation values (HU) and ratio (β -TCP/ host cancellous bone) of CT attenuation values between postoperative 3 and 12 months.

	3 month	12 month	P value
Normal	143 (28-235)	138 (32-224)	0.212
β -TCP	1400 (648-1793)	1011 (527-1451)	< 0.001
β -TCP / host cancellous bone	12.26 (5.37-53.2)	8.37 (3.75-22.50)	0.012

Values are expressed as means with ranges in parentheses.

months to 12 months in all cases (Table 2). The modified van Hemert's grade at postoperative 3 months (2.3 ± 0.9 , range 1 to 4) significantly changed at postoperative 12 months (4.4 ± 0.7 , range 3 to 5) ($P < 0.001$). The mean ratio (β -TCP/host cancellous bone) of CT attenuation values significantly changed from postoperative 3 months to 12 months ($P = 0.012$) (Table 3). Preoperative mFTA (average 4.1° varus) was significantly different from postoperative 3 months (average 4.8° valgus) and 12 months mFTA (average 4.3° valgus) ($p < 0.001$), while no difference was found between postoperative 3 and 12 months ($P = 0.075$) and the IKDC, WOMAC and VAS pain scores significantly improved after surgery ($P < 0.001$, $P = 0.002$ and $P = 0.002$ respectively) (Figures 1-4).

Discussion and Conclusion

The aim of this study was to evaluate the bone union progress and clinical outcome after MOWHTO using injectable β -TCP as osteotomy gap filler. Our initial hypothesis was confirmed that MOWHTO using the injectable β -TCP resulted in satisfactory bone union and clinical result. Serial radiographs showed satisfactory bone union and maturation of β -TCP and serial CT scans showed decreased ratio (β -TCP/host cancellous bone) of CT attenuation values that suggests resorption of β -TCP. Our findings concur with previous reports that showed maturation of graft with bone union after MOWHTO using β -TCP [7-9,13,14].

The need for any spacer or filler to fill the osteotomy gap is an issue still on debate. Various studies reported successful clinical and radiographic outcome after MOWHTO without any spacer [15,16]. In contrast, problems including early loss of correction, delayed bone union and failure of fixative also have been reported [4,17]. In general, autogenous bone graft is considered as the most certain filling material; however, increased operative time or donor site morbidity is not a minor problem. Allogenic bone grafting also is not free from problems like infection or disease transmission. Bone substitutes are used as alternatives in expectation of enhancing initial mechanical stability and shortening bone healing time without additional donor site issue. The β -TCP and hydroxyapatite (HA) are representative among various bone substitute and successful results using β -TCP or HA to fill the osteotomy gap in MOWHTO have been reported

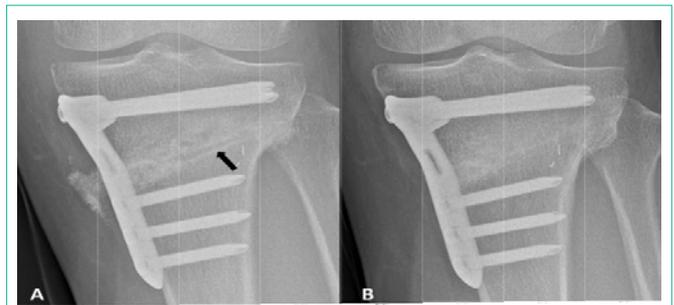


Figure 2: Anteroposterior radiograph of 53-year old woman taken at postoperative 3 months (A) and 12 months (B). Bone union and maturation of β -TCP was evaluated using the modified van Hemert's grade. (A) Blurred distinction between osteotomy line and β -TCP was seen (black arrow) and defined as grade 2. (B) Full reformation of β -TCP was seen and defined as grade 5.



Figure 3: Computed Tomography (CT) images of 53-year old woman showing the center of the osteotomy plane at postoperative 3 months (A) and 12 months (B). The CT attenuation values (in Hounsfield units: HU) of the host cancellous bone area (a) and the injected β -TCP area (b) changed from 89 and 1327 at 3 months to 74 and 666 at 12 months. The ratio (β -TCP/host cancellous bone) of CT attenuation values was 0.067 (3 months) and 0.111 (12 months).

[5,6,18-20]. Both β -TCP and HA is known to be biocompatible and has osteoconductive potential, however, several studies reported that β -TCP has relatively superior resorption rate and osteoconductivity compared to HA [7,21-23]. The reason for this has been suggested that β -TCP has micropores which provide microenvironment for osteoblastic cell formation [21,24]. The absorbability of β -TCP varies according to the porosity that bone formation and resorption were superior with β -TCP of 75% porosity than 60% porosity [8,14]. In our study, we used β -TCP with 75% porosity and bone formation and resorption at postoperative 12 months was satisfactory.

Solid bone substitute wedge is generally used for spacer, since it is easy to handle and might add initial mechanical stability. However, wedge filler covers only part of the osteotomy gap since it is pre-shaped. Also, using solid bone substitute may prevent hematoma leakage which is a mechanism proposed to enhance bone healing and may delay bone in growth due to dense structure [9]. Meanwhile, using granule type bone substitute has theoretical advantage that it may cover a large area of cancellous bone in the open wedge gap and provides a loose matrix for bone in growth. On the other hand, concern remains that granule type bone substitutes can only provide weak mechanical support. Since the advent of anatomical locking plate enabled rigid fixation and decreased the concern of early collapse after MOWHTO [25], we supposed that using injectable

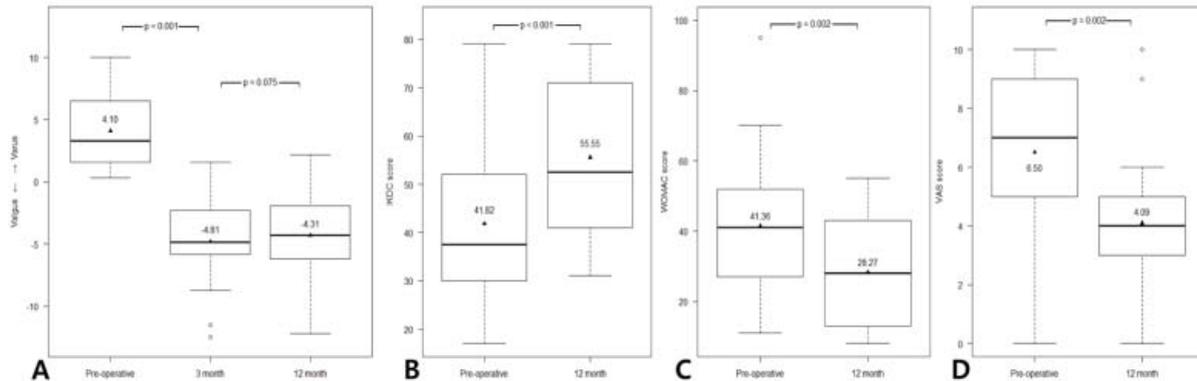


Figure 4: Changes of alignment and outcome scores. (A) Mechanical Femoro-Tibial Angle (mFTA), (B) International Knee Documentation Committee (IKDC), (C) Western Ontario and McMaster Universities Arthritis Index (WOMAC) and (D) visual analogue scale (VAS) for pain scores. Paired t-test.

β -TCP granule combined with locking plate would have benefits. In addition, the injectable β -TCP we used in this study was relatively easy to handle and possible to adjust the shape during the surgery. One thing should be noted that injectable filler may extensively cover the osteotomy surface which may cause limited hematoma formation and delayed bone union. Fortunately, uneventful bony union was achieved in this case series and we assume that higher porosity of the injectable β -TCP granule might have minimized this problem.

This study has several limitations. First, this study is a case series without any control group. It is beyond the scope of our study to conclude whether using β -TCP has any advantage over other gap filler or osteotomy without filling material. Our finding only suggests that β -TCP is safe with satisfactory bone union as gap filler after MOWHTO. Second, three patients who failed to take either postoperative 3 or 12 months CT was excluded from the analysis. Although CT data were not available, those 3 patients were not lost from the follow-up and bony union was achieved uneventfully after postoperative 12 months. Third, longer term effect of injected β -TCP on maintaining the correction angle and functional outcome is uncertain, even though early clinical outcome and bone union rate were satisfactory. Finally, although different sizes of osteotomy gap were needed for each case, we injected same amount of β -TCP. There is possibility that we might have injected excessive β -TCP and vice versa. However, deciding adequate amount of β -TCP depend on the size of osteotomy gap was beyond the scope of our study.

In conclusion, we found satisfactory bone union and clinical outcome without any complication after using injectable β -TCP for MOWHTO. We suppose that injectable β -TCP has theoretical merits including superior bone formation, earlier resorption and easy to handle. Therefore, it can be an effective option as gap filler for MOWHTO when combined with rigid locking plate fixation.

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