

Case Report

Two Cases of High Tibial Osteotomy in Patients with Rheumatoid Arthritis Treated with Biologic Disease-modifying Anti-rheumatic Drugs

Yasuhiro Takahara^{a*}, Keiichiro Nishida^b, Hirotaka Nakashima^a, Nobuaki Ochi^a,
Yoichiro Uchida^a, Hisayoshi Kato^a, Satoru Itani^a, Makoto Nakamura^a,
Yuichi Iwasaki^a, and Yoshitaka Tsujimura^a

^aDepartment of Orthopedic Surgery, Nippon Kokan Fukuyama Hospital, Fukuyama, Hiroshima 721-0927, Japan,

^bDepartment of Orthopaedic Surgery, Okayama University Graduate School of Medicine,
Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan

High tibial osteotomy (HTO) procedure is generally contraindicated in rheumatoid arthritis (RA) patients because synovial inflammation may exacerbate joint damage post-surgery. The natural course of joint destruction in RA changed dramatically with new treatment strategies and the introduction of biologic disease-modifying anti-rheumatic drugs (bDMARDs). We report the cases of two RA patients who underwent HTO and whose disease activities were well controlled by bDMARDs. Despite their short follow-up periods, they showed acceptable objective and subjective clinical results. We believe that the combination of bDMARDs and HTO can be indicated for selected RA patients before total knee arthroplasty.

Key words: high tibial osteotomy, rheumatoid arthritis, biologic DMARD, knee surgery

Since the 15 years after the introduction of biologic disease-modifying anti-rheumatic drugs (bDMARDs) for clinical application in Japan, the bDMARDs have shown promising clinical effects against the disease activity of rheumatoid arthritis (RA) [1]. In addition to a dramatic suppression of synovial inflammation, bDMARDs have been demonstrated to prevent joint destruction and to achieve a structural repair of the joint in some patient populations. However, even under good disease control by bDMARDs, some patients show continuous inflammation of a specific joint, and other patients might already have joint destruction with irreversible functional impairments [2]. Even after the amelioration of synovial inflammation by a bDMARD, joints with hyaline cartilage wear can undergo osteoarthritic changes including osteophyte formation, which can be a cause of joint pain and

a restricted range of motion [3].

The high tibial osteotomy (HTO) procedure has been widely accepted for medial knee osteoarthritis (OA) since Coventry first reported favorable outcomes in 1979 [4]. A few later modifications including open-wedge HTO (OWHTO) [5,6] and lateral closed-wedge HTO (hybrid CWHTO) [7] have contributed to the shortening of the post-operative rehabilitation period. HTO has been contraindicated in patients with RA because poor disease control may lead to a post-operative exacerbation of joint deterioration. However, when the patients are appropriately selected, joint-preserving surgery of the knee joint might be beneficial. Herein we report our experiences with two patients who underwent HTO and whose RA activity was controlled by bDMARDs. These cases demonstrate that a combination therapy of orthopedic surgery and medical treatment can be beneficial for the preservation of the rele-

Received April 2, 2019; accepted July 22, 2019.

*Corresponding author. Phone: +81-84-945-3106; Fax: +81-84-945-3564
E-mail: yasuhiro_takahara@nkfh.or.jp (Y. Takahara)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

vant joints' structure and function.

Case Reports

Case 1. A 71-year-old Japanese woman (height 146 cm, weight 48 kg, BMI 22.6 kg/m²) had developed symptoms of RA at approx. 60 years of age. There was no remarkable past medical history other than the RA. She had been treated with infliximab (200 mg/8 weeks) from 2006 to 2012 and was first prescribed etanercept (50 mg/week) in January 2014 because her condition became refractory. In January 2015, she began receiving tocilizumab (400 mg/4 weeks) followed by abatacept (500 mg/4 weeks) in December 2015 to address the gradual weakening of the effects of previous medications. In 2016, she began receiving methotrexate (MTX, 10 mg/week), abatacept (125 mg/week), and prednisolone (PSL, 2.5 mg/day) to maintain disease control of the RA.

The rheumatology department referred this patient to the orthopedic surgery department because she experienced right knee pain and consequent gait difficulties. At the initial examination, her C-reactive protein (CRP) level was 0.25 mg/dL, anti-cyclic citrullinated peptide antibody (ACPA) level was 124 U/mL, rheumatoid factor (RF) was 25 U/mL, and disease activity score (DAS)-CRP was 2.8: tender joint count: 1, swollen joint count: 1, patient's global assessment of health (PtGA) with the visual analogue scale (VAS): 40. The right knee joint range of motion was -5° - 120° , and the Japanese Orthopedic Association score (JOA score) was 80 points.

Radiographic examinations showed narrowing and osteophyte formation at the medial joint space of right knee. The joint space was preserved at the patella-femoral joint (Fig. 1). The mechanical axis (%MA) was 22%, the standing femoro-tibial angle (FTA) was 180.1° , and the medial proximal tibial angle (MPTA) was 84.2° . An initial arthroscopic assessment revealed that the condition of the lateral cartilage was maintained despite damage to the medial cartilage on both the femoral and tibial condyles, and there was no synovial proliferation in the knee (Fig. 2). Consequently, treatment for ordinary osteoarthritis (OA) was considered, and we performed 10° open-wedge HTO (Fig. 3A). From the day after operation, the patient began range-of-motion (ROM) exercise of the knee and walked with 1/3 partial weight bearing (PWB). She could walk with full weight bearing (FWB) within 4 weeks after the OWHTO.

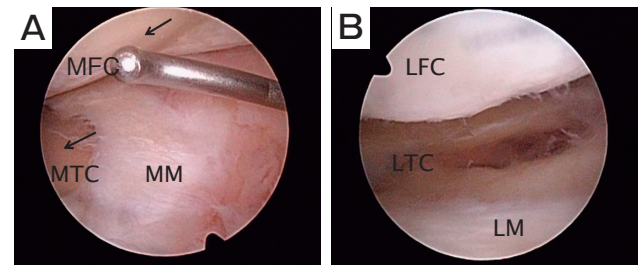


Fig. 2 Arthroscopic findings. **A**, Medial compartment; **B**, Lateral compartment. *Arrow* indicates cartilage loss at the medial femoral and tibial condyles; LFC, lateral femoral condyle; LM, lateral meniscus; LTC, lateral tibial condyle; MFC, medial femoral condyle; MM, medial meniscus; MTC, medial tibial condyle.

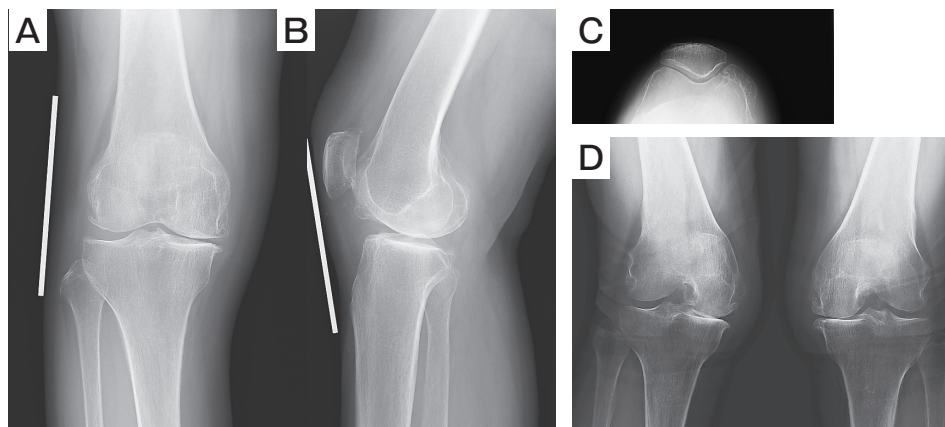


Fig. 1 Case 1. Radiograph before operation. **A**, AP; **B**, lateral; **C**, skyline; **D**, Rosenberg view.

At 20 months postoperatively, the patient exhibited ROMs in the right knee joint of 0° during extension and 135° during flexion while free walking as well as JOA score of 90 points. Successful bone union was achieved, and the medial joint space was maintained (Fig.3B). When the plate was removed, there was no synovial proliferation in a second-look arthroscopic assessment. We also observed no synovial proliferation by MRI after

the plate removal (Fig.3C). The %MA, standing FTA, and MPTA were 60%, 173.2°, and 92.0° at the final follow-up. The patient also exhibited an improved score on the Short Form Health Survey (SF-36), which is used to evaluate patients' satisfaction with their physical and mental states (Fig.4). Currently, the patient's disease activity evaluated using DAS28-CRP is 2.4 (tender joint count: 1, swollen joint count: 0, PtGA: 18, and CRP:

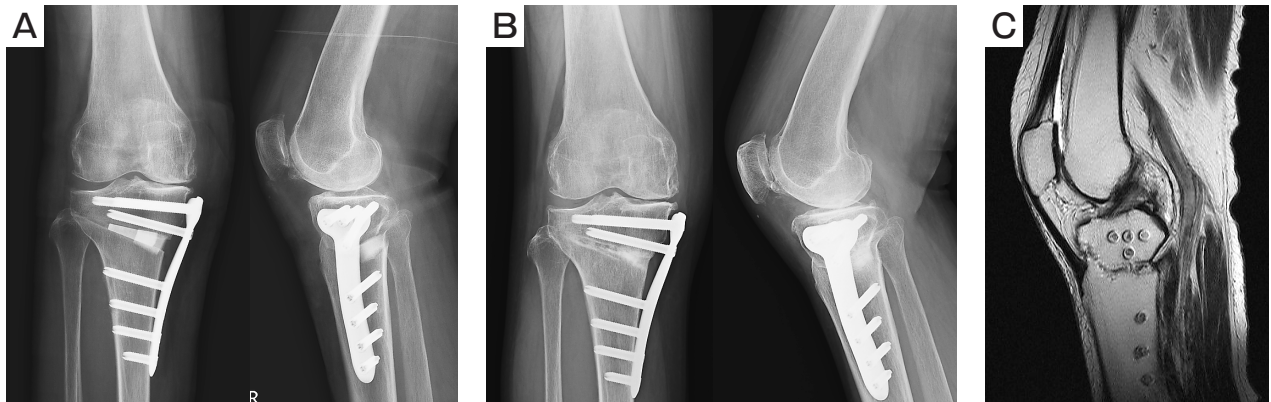


Fig. 3 Postoperative radiograph. A, Just after operation; B, One year after operation, bone union had occurred; C, MRI after implant removal.

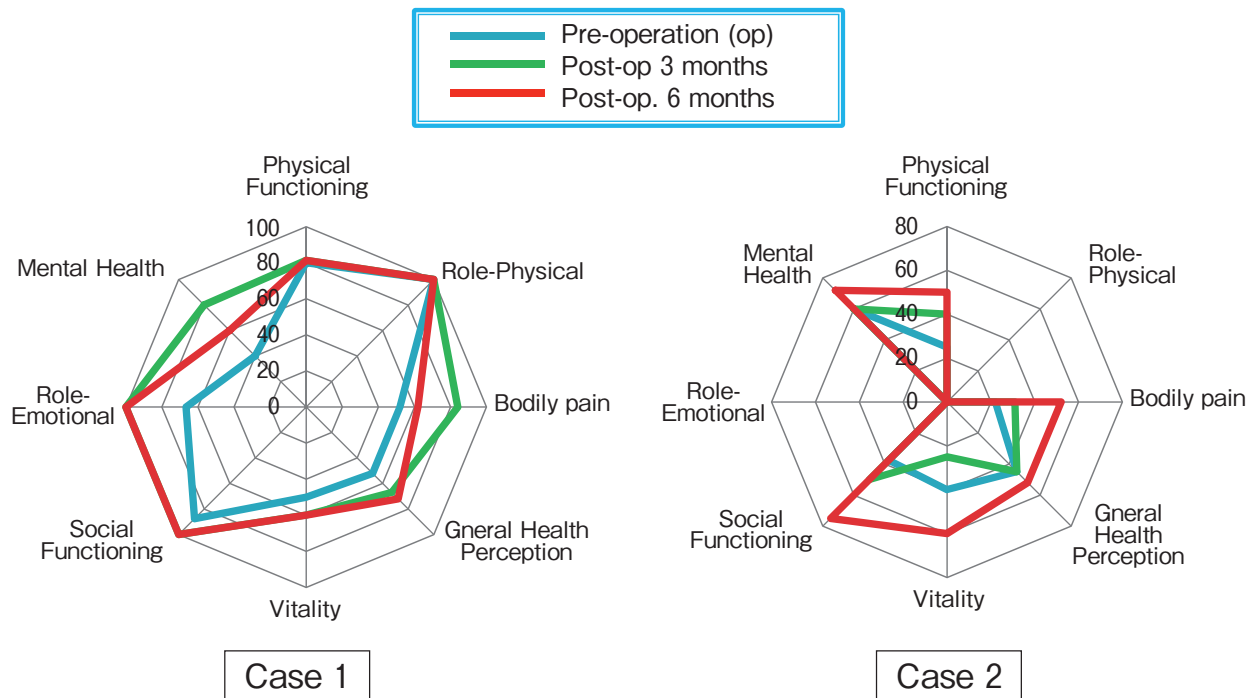


Fig. 4 The changes in the patient's SF-36 scores from before the operation to 3 and 6 months later.

0.55 mg/dL).

Case 2. A 68-year-old Japanese woman (height 155 cm, weight 66 kg, BMI 27.4 kg/m²) had developed RA at approx. 66 years old. There was no notable past medical history other than her RA. A physician had prescribed MTX (4 mg/week) and golimumab (50 mg/4 weeks). She experienced persistent pain in her left knee and was subsequently referred to the department of orthopedic surgery at our hospital in August 2016.

At the initial examination, her CRP level was 8.4 mg/dL, ACPA level was 123 U/mL, RF level was 22 U/mL, and DAS28-CRP was 4.3. As she did not desire injections, she was accordingly prescribed MTX (4 mg/week), golimumab (50 mg/4 weeks), and PSL (5 mg/day).

By January 2017, the patient's CRP level was 1.0 mg/dL and her disease activity evaluated using the DAS28-CRP was 3.1 (tender joint count: 2, swollen joint count: 0, PtGA: 40). Her left knee had a range of motion of -10°-135°, and her JOA score was 50 points. Radiographic examinations showed narrowing and osteophyte formation at the medial joint space. Joint space was preserved at the patella-femoral joint (Fig. 5). The %MA was 25%, the standing FTA was 180.2°, and the MPTA was 85.8°.

An initial arthroscopic assessment revealed cartilage loss on the medial femoral and tibial condyles and synovial proliferation at the anterior capsule (Fig. 6), but the condition of the lateral cartilage was maintained. We performed a synovectomy at the anterior capsule and suprapatellar pouch, followed by a 9° hybrid CWHTO (Fig. 7A). From the day after operation, the patient began ROM exercise of the knee and walked with 1/3 PWB within 1 week. She could walk with FWB within

5 weeks after the hybrid CWHTO.

At 21 months postoperatively, the patient exhibited right knee ROMs of 0° during extension and 135° during flexion while free walking and a JOA score of 70 points. Successful bone union was achieved, and the medial joint space has been maintained (Fig. 7B). When the plate was removed, there was still synovial proliferation at the supra-patellar pouch revealed by a second-look arthroscopic assessment. We also observed some synovial proliferation by MRI after the plate removal (Fig. 7C). The %MA, standing FTA, and MPTA were 61%, 171.6°, and 92.2° at the final follow-up. The patient also exhibited an improved SF-36 score relative to the surveys administered preoperatively and at 3 and 6 months postoperatively (Fig. 4). Her disease activity evaluated using the DAS28-CRP was 1.6 (CRP: 0.66 mg/dL, tender joint count: 0, swollen joint count: 0, PtGA: 0).

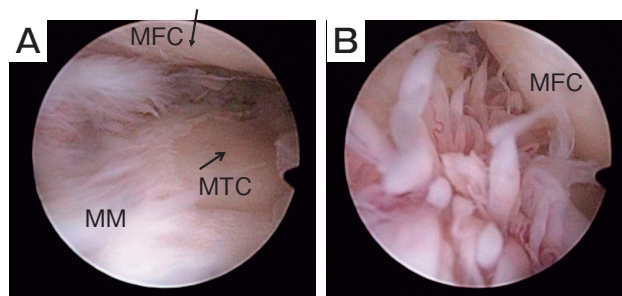


Fig. 6 Arthroscopic findings. **A**, Medial compartment. Arrow indicates cartilage loss at the medial femoral and tibial condyles; **B**, Synovium proliferation at the anterior capsule; MFC, medial femoral condyle; MM, medial meniscus; MTC, medial tibial condyle.

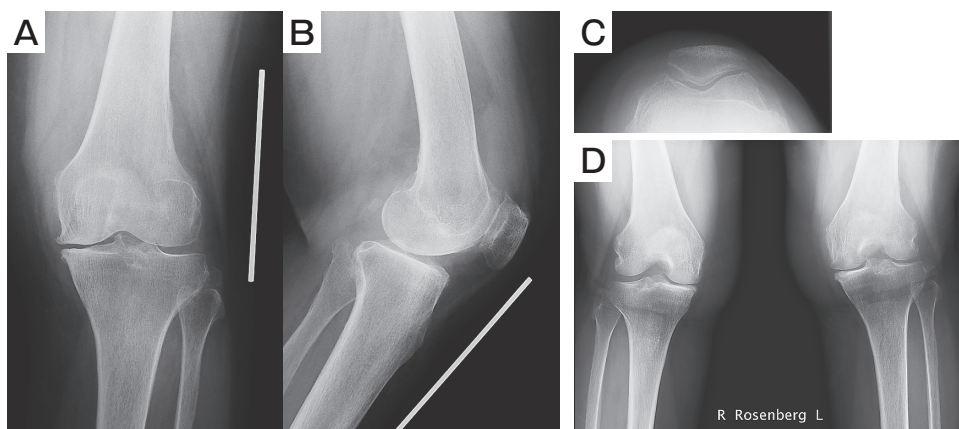


Fig. 5 Case 2. Radiograph before operation. **A**, AP; **B**, lateral; **C**, skyline; **D**, Rosenberg view.

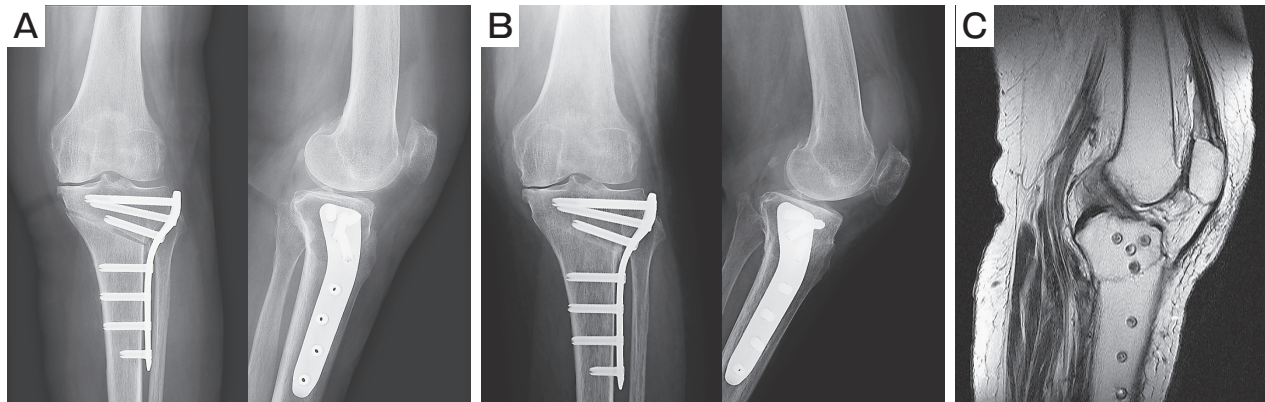


Fig. 7 Postoperative radiograph. **A**, Just after operation; **B**, One year after operation, bone union had occurred; **C**, MRI after implant removal. There was still synovial proliferation at the supra-patellar pouch.

Discussion

In the past, the knee surgeries performed for patients with RA were largely passive with the use of procedures such as artificial joint replacement when the pain became difficult to endure and activities of daily living could no longer be performed. However, if the suppression of joint deterioration can be achieved with medication, more challenging surgical procedures might be considered to further improve the function [8]. The paradigm of surgical reconstruction of a rheumatoid forefoot, which was previously typified by the earlier Lelièvre procedure, has shifted to joint preservation surgery [9-11]. We believe that if knee joint deterioration can be suppressed by biologic drugs, clinicians can consider joint preservation surgeries that are intended to yield more aggressive functional recoveries.

At our institute, HTO has been indicated for OA patients of all ages who exhibit varus limb alignment, localized medial compartment lesions, and knee pain persisting after 3 months of conservative treatment. As HTO is a physiological procedure and requires careful post-treatment care, patients indicated for HTO should be those who can understand and perform post-operative rehabilitation and express a desire for joint preservation. Cases involving infection, pronounced deformation of the patellofemoral joint, a femoro-tibial angle $\geq 185^\circ$, flexion contracture of $\geq 20^\circ$, or a restricted range of motion of $< 90^\circ$ are contra-indication for an HTO. There is no age restriction or BMI restriction among our indications for HTO. It is important for surgeons to note that patient education is essential for successful

postoperative rehabilitation after an HTO.

Very few reports have discussed HTO in patients with RA. Chan *et al.* [12] reported the outcomes of HTO in 36 patients with RA from postoperative years 1 to 6, and they reported that 42%, 19%, and 38% of the outcomes could be classified as good, satisfactory, and poor, respectively. Despite these largely favorable results, however, the prevalence of poor cases increased after postoperative year 3, and the performance of HTO for RA was reported to be inferior to that of HTO for OA symptoms. Additionally, Matsushita *et al.* [13] reported the presence of changes in weight-bearing joints in RA patients who received tumor necrosis factor (TNF) inhibitors based on X-ray assessments. In that report, the Larsen grade [14] (a measure applied to radiographs of RA patients) at treatment initiation and disease activity 1 year later were shown to influence the progression of hip and knee joint deterioration displayed via radiographs. We therefore believe that the sufficient control of RA symptoms is essential when performing HTO surgery in the affected patients.

It is also critical to determine whether an HTO is indicated for a knee joint at the early stage of joint deterioration. Considering our 2 patients, there was no synovial proliferation at the initial arthroscopic assessment in Case 1. We could perform an HTO as OA changed knee in RA patients. In contrast, There was still synovial proliferation in Case 2, and her JOA score and SF-36 improved after the operation but the result was not as satisfactory compared to that of Case 1. An HTO can be indicated in patients with RA only when the disease activity is controlled through a bDMARD

and a lesion originating from medial knee OA is identified through radiographic examinations. The absence of synovial proliferation is the key to achieve satisfactory results of an HTO for an RA patient.

Surgeons should aim for better surgical outcomes and functional improvement for highly demanded patients with better disease control by biologic DMARDs. In recent years, reports have described a fairly low level of patient satisfaction following total knee arthroplasty (TKA) [15]. In the present cases, the SF-36 was used to evaluate the patients' stance type, and it also demonstrated improvements in mental and physical items. Although we have presented the cases of only 2 patients with short postoperative observation periods, we believe that the HTO as a joint-preservation surgery procedure will yield further functional improvements in patients with RA.

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