

Results of Medial Open Wedge High Tibial Osteotomy With 5 Years Follow-Up: A Prospective Multicenter Cohort Study

Takeshi Sawaguchi¹, Sabine Goldhahn², Ryohei Takeuchi³, Ryuichi Nakamura⁴

¹ Department of Traumatology, Fukushima Medical University, Shinyurigaoka General Hospital, 255 Furusawa, Aso-ku, Kawasaki City, Kanagawa, 215-0026 Japan;

² ETH Zurich, Department of Health Sciences and Technology, SLA C5, Schorenstrasse 16, 8603 Schwerzenbach, Switzerland;

³ Saiwai Tsurumi Hospital, 21-1 Toyookacho, Tsurumi-ku, Kawasaki, Kanagawa, 2130-0062 Japan;

⁴ Harue Hospital, Harue-cho Haribara 65-7, Sakai city, 919-0476, Japan.

Conflict-of-interest statement: The authors TS, RT, and SG declare that they had no direct financial support from the sponsor Synthes GmbH for the submitted work. The institution of SG was the contract research organization for this study and was paid for the planning, for monitoring including travel to study-related meetings, for the study analysis, and for writing the manuscript. RN declares that he received fees for travel to study meetings, and for participation in review activities from the sponsor by Synthes GmbH. The authors TS, RT and SG declare that they have no other relationships or activities that could appear to have influenced the submitted work. RN declares that he has a consultancy agreement with Olympus Terumo Biomaterials.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Takeshi Sawaguchi, M.D. Ph.D., Trauma and Reconstruction center, Shinyurigaoka General Hospital, 255 Furusawa, Aso-ku, Kawasaki City, Kanagawa, Japan.

Telephone: + 81 (0) 44 322 9991

Email: sawaguch@mxq.mesh.ne.jp

Received: February 16, 2022

Revised: March 12, 2022

Accepted: March 16 2022

Published online: May 6, 2022

ABSTRACT

AIM: The purpose was to assess whether open wedge high tibial osteotomy (OWHTO) achieves good functional and radiological results until 5 years follow-up.

MATERIALS AND METHODS: A prospective multicenter study in 118 patients 40 years of age and older with osteoarthritis (OA) or osteonecrosis evaluated the outcome after OWHTO using locking plate fixation (TomoFix Medial High Tibial Plate (MHT)[®] small plate: Synthes GmbH, Oberdorf, Switzerland). This paper discusses patient-reported and functional outcomes, radiological results and adverse events after 5 years follow-up. Adverse events (AEs) were evaluated by a complication review board and classified according to a standard classification system, and radiographs were analyzed by study-independent surgeons.

RESULTS: Significant improvement from baseline was observed in the Knee Injury and Osteoarthritis Outcome Score (KOOS), Oxford Knee Score (OKS), Japanese Orthopaedic Association knee score, range of motion, and SF-36 Physical Component Summary (PCS). The anatomical alignment achieved after the OWHTO remained stable over the 5-year follow-up period. The radiologically assessed status of OA (Kellgren-Lawrence) and joint space width narrowing progressed significantly between baseline and five years. The estimated risk of developing at least one local postoperative implant/surgery, bone, or soft tissue AE was 5.1% (95%CI: 1.9; 10.7), 15.3% (95% CI: 9.3; 23.0), and 12.7% (95%CI: 7.3; 20.1), respectively.

CONCLUSION: Function, pain and quality of life can improve during the period of five years despite a structural progression of OA in patients after medial OWHTO.

Key words: "Osteotomy"[MeSH]; Open-wedge; "Osteoarthritis, knee"[MeSH]; Plate; Patient-reported outcome

© 2022 The Author(s). Published by ACT Publishing Group Ltd. All rights reserved.

Sawaguchi T, Goldhahn S, Takeuchi R, Nakamura R. Results of Medial Open Wedge High Tibial Osteotomy With 5 Years Follow-Up: a Prospective Multicenter Cohort Study. *International Journal of Orthopaedics* 2022; 9(2): 1632-1640 Available from: URL: <http://www.ghrnet.org/index.php/ijo/article/view/3293>

INTRODUCTION

Knee osteoarthritis (OA) is a major public health issue that causes chronic pain and disability of the elderly. In Japan, this is a frequent Orthopaedic indication due to the combination of two independent risk factors: genetic predisposition and common method of sitting with maximally flexed knees and parallel position of both legs^[1,2]. Even in the healthy Japanese population, a varus alignment of the knee is more common than in other populations and results in the risk of higher loading of the medial tibiofemoral compartment^[3].

In patients with symptomatic knee OA and varus malalignment, the correction of the mechanical axis is a widely used surgical treatment option that can improve the loading pattern between the medial and lateral knee compartment^[4,5]. Open wedge high tibial osteotomy (OWHTO) has the goal to improve pain and function and reduce progression of joint degeneration in knee OA primarily located in a single knee compartment^[4,6]. Studies suggest that this concept can result in good functional and radiological results and low complication rates^[7-10]. The long-term goals of an OWHTO are to keep the patient's activity and to delay the need for joint replacement.

The TomoFix Medial High Tibial Plate (MHT)[®], small plate (Synthes GmbH, Oberdorf, Switzerland) was designed to overcome previous implant-associated limitations such as mismatch of the shape and bulkiness in medial OWHTO in East-Asian patients who have different anatomic dimensions of the tibiae compared to Caucasian patients^[3,11]. Advantages of this implant type include reduced operative time, improved periosteal blood supply and subsequent healing, prevention of primary and secondary loss of correction, and finally, improved functional outcomes, and reduced pain^[10,12-15]. Prospective studies assessing long-term outcome after medial OWHTO using the TomoFix plate for small stature patients are still lacking.

Here we report the functional, radiological, and safety 5-year results of the surgical arm of a prospective, multicenter cohort study that was conducted in 118 Japanese patients with medial unicompartmental OA and/or osteonecrosis (ON) of the knee who had an indication for OWHTO with plate fixation. The primary objective of the study was to evaluate whether the functional outcome as measured by the Knee Injury and Osteoarthritis Outcome Score (KOOS) at the 2-year follow-up was better in patients who underwent surgery than in patients who declined surgery and continued with non-surgical or no treatment. While results of this 2-year follow-up have been reported^[16], the current analysis addresses the question whether the observed positive effect of OWHTO with the plate can be maintained up to 5 years without the need for treatment conversion. The analysis focuses on patient-reported outcomes as well as radiological signs for disease progression. Additionally, a comprehensive analysis of treatment/implant-related complications can add to the evidence to improve the surgical technique.

METHODS

The study was approved by the ethics committees of the nine participating clinics. To be eligible for inclusion in this prospective multicenter cohort study, patients 40 years of age and older were required to have either medial unicompartmental OA Grade 1 to 4 (Kellgren-Lawrence) or ON stage 2 to 4 (Koshino classification) of the knee^[17]. Patients were excluded if they met any of the following exclusion criteria: ligamentary laxity, femoro-tibial angle (FTA) > 190° in standing X-ray view, flexion contracture > 15°, total knee replacement or unicompartmental knee on the contralateral side,

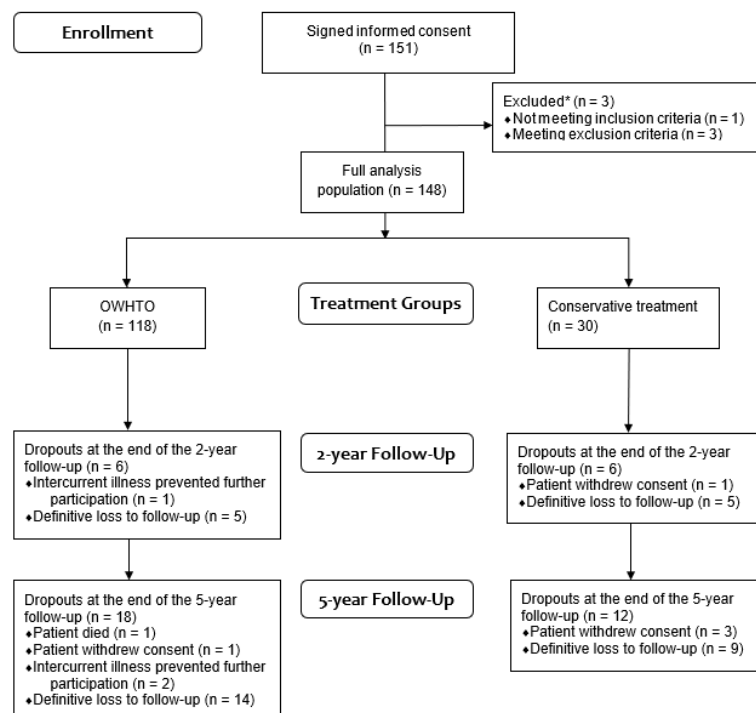


Figure 1 Patient recruitment flow diagram. *both groups

severe OA or surgery of the hip joint, reconstruction of anterior or posterior cruciate ligament of the same knee, severe OA of the ipsilateral ankle joint, infections located between the middle of the femur and the ankle, and smoking of more than 20 cigarettes per day.

Patient demographics

A total of 148 patients were enrolled in the study after giving written informed consent. Of these patients, 118 underwent OWHTO surgery (OWHTO group) and 30 declined surgery, i.e., commenced or continued with conservative treatment. Because of the small group size of this conservative control group with 12 dropouts (40%) during follow-up, and imbalances in the distribution of the baseline characteristics, this paper discusses the study results at 5 years follow-up for the OWHTO group. Results for the conservative group are presented in supplemental material Additional file 1.

The mean (SD) age of the OWHTO group was 64.7 ± 8.4 years (range: 42.0-79.0 years). The majority of these patients were female ($n = 99$, 83.9%), non-smokers ($n = 110$, 93.2%) and unable to sit in Japanese style prior to surgery ($n = 104$, 88.1%). At baseline, 26 patients suffered from both OA and ON whereas one patient had ON only. In 88 patients (74.6%), OA of Kellgren-Lawrence Grade 2-4 was observed. Detailed baseline characteristics are available in the 2-year results previously reported^[16]. By the 5-year follow-up, 18 patients had discontinued the study and 100 (84.7%) patients had completed the final follow-up after their OWHTO (Figure 1).

Surgical intervention and subsequent rehabilitation

The OWHTO plate procedure was performed according to Staubli and Lobenhoffer^[12,15] with the goal to achieve postoperative anatomical valgus angulation of 10° (FTA of 170°) or restoration of the mechanical axis with a weight-bearing line ratio (WBL-ratio) at 62.5% of the tibial plateau.

One hundred and three patients (88.0%) with OWHTO had a knee arthroscopy at the beginning of the OWHTO surgery, 14 patients (12.0%) as a separate procedure before. The mean Chondropenia Severity Score (CSS) at baseline was 62.8 ± 12 (range: 32.0-

88.0)^[18,19]. Medial meniscectomy was performed on 76 patients (64.4%), and 29 patients (24.6%) had osteophytes removal during the arthroscopic examination. The optional procedures of drilling, microfractures or notchplasty were performed in 25 (21.2%), 7 (5.9%) and 5 (4.2%) patients, respectively. The mean opening distance of the osteotomy gap at the medial side was 11.2 ± 2.4 mm (range: 6.0-20.0). The osteotomy site was optionally filled with β -tricalcium phosphate wedges (Osferion 60[®], 60% porosity [Olympus Biomaterial, Tokyo, Japan]) as bone substitute in 27.1% ($n = 32$) of cases. Patients with gap filling were recommended to start partial weight-bearing immediately after surgery and full weight-bearing approximately 10 days after surgery. Patients without gap filling were recommended to start active and passive range of motion and muscle strengthening exercises the day after surgery. The start of partial weight-bearing was recommended within two weeks after surgery with the aid of a walker and full weight-bearing was recommended for all patients within six weeks of the OWHTO procedure^[20]. Patients with radiologically detected lateral hinge fractures type 1 to 3 ($n = 53$) started 15 days later with free full weight-bearing than patients without a lateral hinge fracture^[21,22].

One-hundred and six patients had a second-look arthroscopy. One-hundred and nine patients (97.3%) had an implant removal after a mean of 21 ± 4.7 months (range: 5.0-28.0). Implant removal was foreseen to be performed at the 2-year follow-up as standard of care after healing but was not obligatory. In case the implant removal had to be performed earlier due to soft tissue or other objective clinical problems it was reported as a complication.

Functional outcome quantification

Patients completed the KOOS and Oxford Knee Score (OKS) and the SF-36 v2 to assess general quality of life, all of which were validated for the Japanese population^[21,23-27]. With respect on the potential impact of a more proximal pathology on functional outcome, the Visual Analogue Scale (VAS) for general/total body pain was included in the evaluation of the prognostic factors for KOOS.

The treating surgeons completed the Japanese Orthopaedic Association (JOA) score for OA knees (consisting of four main items: pain on walking, pain on ascending or descending stairs, range of motion (ROM) and joint effusion) and interviewed patients to determine whether they were able to perform sports and to sit in Japanese style^[28]. Surgeons also evaluated the patient's ROM, processed as absolute and relative (compared to the contralateral side) measure.

Radiological evaluation

The stage of OA or ON was determined on knee full extension standing ap radiographs using the respective Kellgren-Lawrence and Koshino radiographic grading systems^[17,29]. Additional radiological outcomes included the femoro-tibial angle (FTA, standing AP weight-bearing whole leg with knee in full extension X-ray), femorotibial joint space width (measured on a 45° flexed weight-bearing PA X-ray, Rosenberg-position), weight-bearing line ratio (WBLR, calculated from a standing AP whole leg X-ray), tibial slope (lateral weight-bearing knee X-ray) and tibia vara (standing AP knee X-ray). Radiographs were analyzed by study-independent Orthopaedic surgeons.

Complication assessment

Postoperative adverse events (AEs) were categorized as implant/surgery complications, bone complications, soft tissue complications and general/systemic complications in other areas of the body according to a standardized method^[30]. A final classification of all postoperative complications was performed by a complication

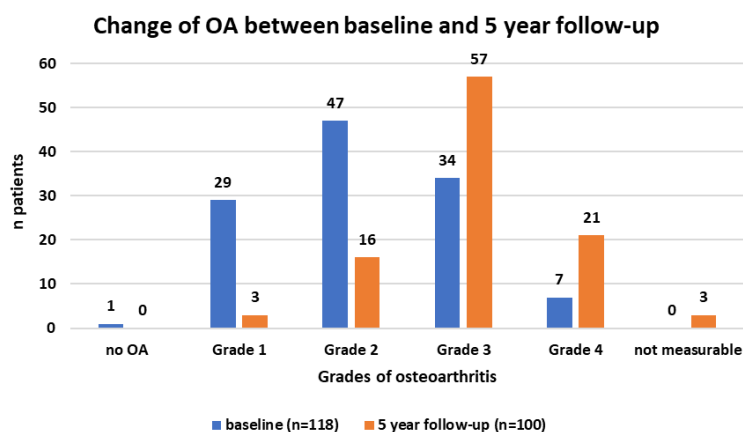


Figure 2 Grades of osteoarthritis (OA) at baseline and 5 years (enrolled OWHTO patients).

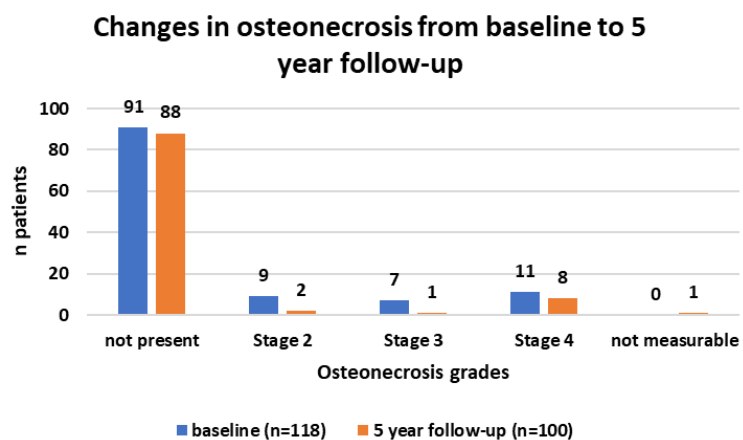


Figure 3 Osteonecrosis grades. At baseline, all except one patient had combined types of osteoarthritis and osteonecrosis.

review board (CRB) composed of the study principal coordinating clinical investigator and two experienced study-independent knee surgeons. For all reported events, a reliability assessment from all three evaluators was recorded at the beginning of the review meeting. Cases without 100% agreement were further addressed in a guided discussion until consensus was reached.

Fractures of the lateral cortex were assessed according to Takeuchi^[22], but only type 2 and type 3 were further examined in the AE analysis because a type 1 fracture heals with slightly delayed weight-bearing and has no further consequences. It is located in or just proximal to the proximal tibiofibular joint and strengthened because of the strong capsular ligament attachment to this area.

Statistical Methods

Change in functional outcomes over follow-up was analyzed using mixed effects models for repeated measures with unstructured covariance, and P values. In addition, confidence intervals for change from baseline were adjusted for multiple testing at several time points with simulation-based approach. Univariable regression model analyses were performed in all patients to assess the effect of potential prognostic factors on KOOS subscale scores at five years.

Change in radiological parameters from baseline to 5 years was analyzed using paired t-tests and Wilcoxon sign rank test.

Adverse events are reported by category at patient level. For the analysis at patient level multiple events of the same type were combined for each patient, and the worst severity or outcome for each event type was presented for the analysis. For AE rates, 95% confidence intervals were calculated using the Clopper-Pearson method.

RESULTS

Functional Outcomes

All KOOS subscale scores improved from baseline to the 5-year follow-up (Table 1) with all five subscales showing a statistically significant change from baseline ($p \leq 0.001$, Table 2).

The influence of different prognostic factors on the KOOS subscale scores is shown in detail in the Additional file 2.

Statistically significant improvement from baseline was also observed in the OKS, the JOA knee score, absolute and relative

Table 1 Summary of the KOOS (sensitivity analysis, data available for both after 2 and 5 years).

Visit	KOOS subscales				
	Pain	Symptoms	ADL	Sports	QOL
n	98	98	98	98	98
Baseline					
Mean (sd)	50.4 (17.1)	55.8 (19.4)	65.3 (15.5)	28.0 (22.1)	29.5 (17.1)
Min; Max	13.9; 83.3	3.6; 92.9	29.4; 97.1	0.0; 80.0	0.0; 81.3
2 years					
Mean (sd)	82.5 (13.5)	81.9 (14.0)	88.4 (10.1)	61.2 (22.8)	67.0 (18.6)
Min; Max	38.9; 100.0	32.1; 100.0	50.0; 100.0	0.0; 100.0	25.0; 100.0
5 years					
Mean (sd)	83.8 (14.4)	81.6 (14.4)	88.4 (11.8)	66.4 (25.6)	71.4 (19.0)
Min; Max	38.9; 100.0	25.0; 100.0	38.2; 100.0	0.0; 100.0	6.3; 100.0

ADL: activities of daily living; KOOS: Knee Injury and Osteoarthritis Outcome Score; QOL: quality of life. Highest score = 100; lowest score = 0.

Table 2 Mean change from baseline in functional and patient-reported outcomes at 5 years (enrolled OWHTO patients).

Outcome	Follow-up	Mean (95% CI)	Mean change from baseline (95% CI)	P value
KOOS Pain	Baseline	49.5 (46.2;52.9)	-	-
	5 years	84.0 (80.9;87.1)	34.4 (29.3;39.6)	<0.001
KOOS Symptoms	Baseline	55.2 (51.6;58.8)	-	-
	5 years	81.8 (78.7;84.9)	26.6 (21.7;31.5)	<0.001
KOOS ADL	Baseline	64.3 (61.3;67.3)	-	-
	5 years	87.9 (85.3;90.5)	23.6 (19.6;27.6)	<0.001
KOOS Sport	Baseline	26.0 (22.0;30.0)	-	-
	5 years	65.6 (60.5;70.7)	39.6 (32.3;47.0)	<0.001
KOOS QOL	Baseline	28.3 (25.2;31.5)	-	-
	5 years	71.3 (67.5;75.1)	42.9 (37.0;48.9)	<0.001
OKS	Baseline	33.8 (32.4;35.3)	-	-
	5 years	19.3 (17.9;20.7)	-14.6 (-16.8;-12.4)	<0.001
JOA	Baseline	64.0 (61.4;66.6)	-	-
	5 years	92.9 (90.9;94.9)	28.9 (25.2;32.6)	<0.001
Absolute ROM	Baseline	126.3 (123.5;129.2)	-	-
	5 years	134.7 (132.4;137.1)	8.4 (4.6;12.2)	<0.001
Relative ROM	Baseline	90.3 (88.5;92.1)	-	-
	5 years	98.6 (97.6;99.7)	8.3 (5.9;10.8)	<0.001
PCS	Baseline	24.1 (21.4;26.7)	-	-
	5 years	41.2 (38.5;44.0)	17.2 (12.6;21.7)	<0.001
MCS	Baseline	51.2 (49.5;52.9)	-	-
	5 years	51.9 (50.1;53.6)	0.6 (-1.6;2.9)	0.929

KOOS: Knee Injury and Osteoarthritis Outcome Score; ADL: activities of daily living. QOL: quality of life; highest score = 100; lowest score = 0. OKS: Oxford 12-item Knee Score; best score = 12, worst score = 60. JOA: The Japanese Orthopaedic Association knee score, best score = 100, worst score = 0. ROM: range of motion. PCS: Physical Component Summary. MCS: Mental Component Summary

ROM, and the SF-36 Physical Component Summary (PCS) while the Mental Component Summary (MCS) remained stable over the period between baseline and five years (Table 2).

The ability to sit in Japanese style improved significantly from baseline to the 5-year follow-up, with an OR (95% CI) of 4.64 (2.06;10.45), $p < 0.001$ at five years. Of the 26 patients with 5-year follow-up who were active in any kind of sports at baseline, 22 (84.6%) were able to do sports at the same level, 3 patients (11.5%) were doing more sports, and one patient (3.8%) did less.

Radiological Outcomes

The radiologically assessed status of OA progressed between baseline and five years. The number of patients diagnosed with grade 2-4 OA (Kellgren-Lawrence grade classification) were 88 patients (74.6%) at baseline and 94 patients (94.0%) at five years (Figure 2).

Shift table analysis of OA status change from baseline to five years showed that the number of patients whose OA became more severe at five years than at baseline was statistically significant ($p < 0.001$).

Twenty-seven patients (22.9%) were diagnosed with stage 2-4 ON (Koshino classification) at baseline, all except one in combination with OA. At five years, this number had decreased to 11 patients (11.0%) (Figure 3).

The radiological analyses of other outcomes revealed significant treatment effects that remained stable over the 5-year follow-up, for example the corrected anatomical alignment with a mean FTA correction of 9.4°, a mean WBLR correction of 41.4%, and a stable change of 9.4° in tibia vara from baseline.

A non-significant change from baseline was observed in tibial slope at 5 years. The joint space width decreased slightly between baseline and five years. Radiological results are summarized in Table 3.

Complications

A total of 88 AEs were reported in 56 (47.5%, 56/118) patients until the 5-year follow-up.

At least one postoperative AE (44.9%) was observed in fifty-three patients; half of them (27 patients) experienced a general/systemic AE in other areas of the body than the affected knee. The estimated

Table 3 Mean change of radiological parameters from baseline to 5 years.

Parameter	n	Mean (95% CI)	Change from baseline, Mean (95% CI)	P value*
FTA (°)				
Baseline	84	179.5 (179.0;180.1)		
5 years	84	170.1 (169.4;170.7)	-9.4 (-10.3;-8.6)	<.001
WBLR (%)				
Baseline	87	22.8 (20.5;25.0)		
5 years	87	64.2 (61.4;67.0)	41.4 (37.7;45.2)	<.001
Tibia vara (°)				
Baseline	89	84.3 (83.9;84.7)		
5 years	89	93.7 (93.1;94.4)	9.4 (8.8;10.1)	<.001
Tibial slope (°)				
Baseline	94	6.98 (6.33;7.64)		
5 years	94	7.15 (6.51;7.78)	0.16 (-0.51;0.83)	0.631
Joint space width (mm)				
Baseline	95	2.37 (2.09;2.66)		
5 years	95	2.04 (1.77;2.32)	-0.33 (-0.55;-0.11)	0.004

Only patients with measurements available at both time points were included. *Paired t-test. FTA values above 180° represent an anatomical varus alignment, FTA values below 180° an anatomical valgus alignment. Cases with flexion contracture of >10° at baseline were excluded.

risk of developing at least one general/systemic postoperative AE was 22.9% (95%CI: 15.7; 31.5). A total of 6, 18 and 15 patients experienced at least one postoperative AE categorized in the respective complication class implant/surgery, bone, and soft tissue. The estimated risk of developing at least one local postoperative implant/surgery, bone, or soft tissue AE was 5.1% (95%CI: 1.9; 10.7), 15.3% (95% CI: 9.3; 23.0), and 12.7% (95%CI: 7.3; 20.1), respectively.

In 38/56 (67.9%) patients with an AE, the event was classified as serious (SAE). In 24 of 27 patients with a general/systemic complication (88.9%), the event was classified as serious. The highest percentage of local postoperative SAEs around the knee was found in the category “soft tissue” (80%, 12/15).

Seven patients (12.5%, 7/118) had an AE that was assessed as likely related to the implant; all of these events were classified under the category “soft tissue” (pain around the plate). The CRB found local AEs (8 intraoperative and 25 postoperative events) that were likely related to the surgical technique in 30 patients.

According to CRB assessment of the most likely cause of the AE, respective 15 (29.4%) and 18 (35.3%) AEs occurred due to wrong positioning of the plate or suboptimal surgical technique. One patient with a three compartmental OA (1%, 1/118) underwent conversion to total knee arthroplasty (TKA) after loss of correction and screw breakage between the head and shaft of the screws after three months. A total of 43 patients with an AE (79.6%) or 65 events (84.4%) recovered without persistent damage. One patient with a general SAE – pancreatic cancer – died.

DISCUSSION

The results of the 5-year follow-up after treatment of knee OA and ON with OWHTO and plate fixation in Japanese patients are reported. The most important finding of this study is that the surgically achieved limb alignment can safely be maintained over five years thus allowing only minimal further joint space narrowing. This provides the base for further functional improvement, e.g., in sports activity, and quality of life from two to five years after OWHTO although the correction of the mechanical axis could not completely stop progression of OA.

Despite the structural progression of OA, the preservation of radiological correction and subsequent improvement in functional activity both led to better quality of life after 5 years demonstrated by an almost doubled PCS of the SF-36 and an increase in the KOOS knee-related quality of life (QOL). The results of this study indicate radiological as well functional improvements in line with the clinical literature^[31,32]. Moreover, this finding helps to link the surgical correction of limb alignment with improved activity, demonstrated by OKS and JOA knee score, and finally social participation, and represents evidence for patient added value. Our results show that both pain relief and functional restoration are already achieved two years after OWHTO but return to sports and quality of life continue to improve up to five years after surgery. Especially return to sports shows large interindividual variations five years after surgery and may be attributable to different intensities and frequencies of sports activities.

Results from our study also revealed that several factors significantly impact the functional result of OWHTO. Most of the KOOS subscales are confounded by duration and severity of OA prior to the surgical intervention. BMI at baseline has a significant impact on several KOOS scales. The KOOS subscales Symptoms, activities of daily living (ADL) and Sports, all show a negative correlation to

BMI. In other words, the higher the BMI at baseline is the lower will be the functional outcome. This result is supported by the findings from other authors, who report better cartilage regeneration in patients with lower BMI after second-look arthroscopy and better functional results^[10,33,34]. In line with other researchers, age at baseline did not affect functional results^[33,35]. In our cohort, age contributed only to KOOS Sports five years after OWHTO.

The 5-year follow-up also demonstrates that limb alignment can be maintained over time and joint space narrowing can be effectively minimized. Nevertheless, radiologically measured OA progressed over time indicating that limb realignment cannot completely prevent disease progression. However, radiological progression does not necessarily reflect patient’s condition, and parameters other than those investigated here may play an important role in disease progression and the prediction of clinical improvement^[36-38]. The inflammatory component of OA can contribute in different ways to disease progression or retention^[36]. OA pathogenesis involves not only breakdown of cartilage, but also remodelling of the underlying bone, formation of ectopic bone, hypertrophy of the joint capsule, and inflammation of the synovial lining. However, the inflammatory component of OA was not target of this study and therefore not measured.

In contrast, ON as the second etiology investigated in this study improved over the course of five years. The idea of the HTO is the correction of poor knee alignment and prolongation of the life span of the knee joint by shifting the pressure from the medial, arthritic compartment. This transfers the load to the healthier, lateral knee compartment, and may mitigate the mechanical disruption, which is considered a key pathophysiological factor of ON, as shown in our results. There is a clear shift towards lower ON grades five years after intervention that may indicate regeneration of cartilage as described in other studies^[39].

Limb realignment surgery, especially HTO, is considered an effective method for joint preservation^[4]. Several biomechanical gait studies demonstrated long-term improvements in knee loading during walking^[40,41]. Large reductions of the knee adduction moment as a proxy for mediolateral knee load distribution have been reported up to 5 years and longer after surgical intervention^[32,40]. The changed loading conditions enable cartilage regeneration as demonstrated by second-look arthroscopy or MRI^[31,42]. Consequently, patient-reported outcomes from longitudinal studies have revealed clinically meaningful decreases in pain as well as improvement of function comparable to our study results^[6,43]. Those findings make HTO a cost-effective treatment, especially in middle-aged patients, but also in patients with higher age^[35,44,45]. However, complications, treatment conversions and revisions contribute to costs and represent an important factor in this calculation^[45]. Therefore, a low complication rate is of high importance to favor HTO.

Only one patient (1%) with treatment failure and need for conversion to TKA was observed in our study and reported in detail in the 2-year results^[16]. As the study was designed to assess patients with medial unicompartmental OA and ON of the knee, having enrolled this patient with a tricompartmental knee OA should be considered a study limitation.

No additional treatment failure occurred between 2- and 5-year follow-up. The 99% survival rate at the 5-year follow-up is higher than in another study, where five years after implantation of a Puddu plate a 94% osteotomy survival rate was reported^[46]. A high primary stability of the TomoFix small plate may have contributed to our superior result.

OWHTO has been developed to improve surgical results and

to avoid typical complications such as peroneal nerve palsy or lateral collateral ligament insufficiency reported after other surgical techniques^[7]. OWHTO does not require excessive muscular dissection, fibular osteotomy or peroneal nerve dissection. An overall complication rate from 37% to 55% is reported in the literature^[7]. The overall complication rate of our multicenter study of 47.5% is in the same range. While only 7 postoperative AEs were classified as likely implant-related, 8 intraoperative and 25 postoperative AEs were classified as likely related to surgical technique. These classifications demonstrate on one hand that the TomoFix small plate works well in this patient population but they also show that the main room for improvement is related to surgical technique and can be approached by targeted education. The majority of intraoperative AEs were lateral hinge fractures that did not need additional management or could be addressed during the same procedure. Lateral hinge fractures are known AEs reported after OWHTO. Takeuchi type 1 fractures heal without the need for additional treatment and do not have a negative impact on WBLR or functional results^[47]. The postoperative AEs likely related to surgical technique include loss of reduction, breakage of single screws, delayed healing and local pain. The classification by the CRB as “likely related to surgical technique” indicates that they could have been avoided with the correct surgical procedure as initially described^[12,15]. Correct creation of the open wedge (without additional fracture) as well as optimal placement of the plate both seem the main challenges in this specific technique. Therefore, improved surgical training may help to reduce the amount of intra- and postoperative AEs significantly. Other AEs like wound infection can be addressed with rigorous hygienic regime and local wound treatment. Although almost 80% of patients recovered completely, better surgical training may further increase this number.

Limitations

The main limitation of the study is that it was planned as a comparative cohort study, but could not be analyzed accordingly at the 5-year follow-up due to a number of reasons: first, the baseline characteristics of the conservative group being not comparable, second, the small sample size with low 5-year follow-up in the conservative group, third, the baseline arthroscopy that was also performed in conservative patients and could have had an effect on the outcome, fourth, the diversity of conservative treatment options allowed including no treatment. Because of these reasons, only data of the OWHTO group were discussed. Another limitation of the study is the inclusion of two different pathologies (OA and ON) as an indication for OWHTO. The different underlying pathophysiologies make comparisons or pooling of the results difficult.

CONCLUSIONS

OWHTO using TomoFix small plate is an effective method for limb realignment. Despite a structural progression of OA, function, pain and quality of life improve over a five years follow-up period. Parameters other than those investigated here may play an important role in disease progression and the prediction of clinical improvement and should be investigated in the future.

ACKNOWLEDGEMENTS

Authors' contributions: TS and SG participated in the conception and design of the study, in the overall study coordination, and in the interpretation of data. TS participated in the complication review and revised the manuscript. SG was involved in data analysis and drafted the manuscript. RT and RN participated in the conception of the

study, in data acquisition and revised the manuscript. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

The authors of this study wish to thank the sponsor, Synthes GmbH, Oberdorf (Switzerland) and its representative, Marta Kerstan, as well as Johnson & Johnson K.K. (Japan) for their continuous support. We acknowledge the encouragement by the Joint Preservation Expert Group of the AO Foundation. Our deep gratitude belongs to the participating surgeons Takenori Akiyama (Akiyama Clinic Fukuoka), Kennichi Goshima (Toyama Municipal Hospital), Norimasa Nakamura (Institute for Medical Science in Sports, Osaka Health Science University), Junsuke Nakase (Department of Orthopaedic surgery, Kanazawa University Hospital), Yuzo Yamada (Osaka Hospital), Kenji Yoneda (Moriguchi Keijinkai Hospital, Osaka), and Akihiko Yonekura (Nagasaki University Hospital). In addition, we acknowledge the support of the following hospitals: Akiyama Clinic and Hamanomachi Hospital Fukuoka, Kanazawa University Hospital, Moriguchi Keijinkai Hospital Osaka, Nagasaki University Hospital, Osaka Hospital, Toyama Municipal Hospital, Yawata Medical Center, Yokohama City University School of Medicine, Yokosuka Municipal Hospital. We would like to thank Kathrin Espinoza from AO Innovation Translation Center for performing the statistical analysis. For supporting the radiological analysis, we thank the following surgeons: Adeolu Adeyeye, Amr Eisa, Christoph Heidt, Chumnarn Iamsirikulmit, Akira Nakanishi. We gratefully acknowledge the efforts of the study coordinator Ms. Tomiko Murashita, and the study nurses of the participating clinics.

REFERENCES

1. Koshino T, Saito T, Orito K, Mitsuhashi S, Takeuchi R, Kurosaka T. Increase in range of knee motion to obtain floor sitting after high tibial osteotomy for osteoarthritis. *Knee* 2002; **9**: 189-196. [DOI: 10.1016/s0968-0160(01)00148-x]
2. Muraki S, Akune T, Oka H, Mabuchi A, En-Yo Y, Yoshida M, Saika A, Nakamura K, Kawaguchi H, Yoshimura N. Association of occupational activity with radiographic knee osteoarthritis and lumbar spondylosis in elderly patients of population-based cohorts: a large-scale population-based study. *Arthritis Rheum* 2009; **61**: 779-786. [DOI: 10.1002/art.24514]
3. Tamari K, Tinley P, Briffa K, Aoyagi K. Ethnic-, gender-, and age-related differences in femorotibial angle, femoral antetorsion, and tibiofibular torsion: cross-sectional study among healthy Japanese and Australian Caucasians. *Clin Anat* 2006; **19**: 59-67. [DOI: 10.1002/ca.20170]
4. Lobenhoffer P. The rationale of osteotomy around the knee. *J Knee Surg* 2017; **30**: 386-392. [DOI: 10.1055/s-0037-1603755]
5. Goshima K, Sawaguchi T, Shigemoto K, Iwai S, Nakanishi A, Ueoka K. Assessment of unloading effects after open wedge high tibial osteotomy using quantitative bone scintigraphy. *J Orthop Sci* 2019; **24**: 680-685. [DOI: 10.1016/j.jos.2018.12.020]
6. Birmingham TB, Giffin JR, Chesworth BM, Bryant DM, Litchfield RB, Willits K, Jenkyn TR, Fowler PJ. Medial opening wedge high tibial osteotomy: a prospective cohort study of gait, radiographic, and patient-reported outcomes. *Arthritis Rheum* 2009; **61**: 648-657. [DOI: 10.1002/art.24466]
7. Martin R, Birmingham TB, Willits K, Litchfield R, Lebel ME, Giffin JR. Adverse event rates and classifications in medial opening wedge high tibial osteotomy. *Am J Sports Med* 2014; **42**: 1118-1126. [DOI: 10.1177/0363546514525929]
8. Lind M, McClelland J, Wittwer JE, Whitehead TS, Feller JA, Webster KE. Gait analysis of walking before and after medial opening wedge high tibial osteotomy. *Knee Surg Sports Traumatol*

- Arthrosc* 2013; **21**: 74-81. [DOI: 10.1007/s00167-011-1496-y]
9. Schallberger A, Jacobi M, Wahl P, Maestretti, G, Jakob RP. High tibial valgus osteotomy in unicompartmental medial osteoarthritis of the knee: a retrospective follow-up study over 13-21 years. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 122-127. [DOI: 10.1007/s00167-010-1256-4]
 10. Floerkemeier S, Staubli AE, Schroeter S, Goldhahn S, Lobenhoffer P. Outcome after high tibial open-wedge osteotomy: a retrospective evaluation of 533 patients. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 170-180. [DOI: 10.1007/s00167-012-2087-2]
 11. Tamari K, Briffa NK, Tinley P, Aoyagi K. Variations in torsion of the lower limb in Japanese and Caucasians with and without knee osteoarthritis. *J Rheumatol* 2007; **34**: 145-150.
 12. Lobenhoffer P and Agneskirchner JD. Improvements in surgical technique of valgus high tibial osteotomy. *Knee Surg Sports Traumatol Arthrosc* 2003; **11**: 132-138. [DOI: 10.1007/s00167-002-0334-7]
 13. Lobenhoffer P, DeSimoni C and Staubli AE. Open-wedge high-tibial osteotomy with rigid plate fixation. *Techn Knee Surg* 2002; **1**: 93-105.
 14. Staubli AE. Erster Erfahrungsbericht mit dem Medivision-System 304. *Swiss Surg* 2002; **8**: 50, 163.
 15. Staubli AE, De Simoni C, Babst R, Lobenhoffer P. TomoFix: a new LCP-concept for open wedge osteotomy of the medial proximal tibia--early results in 92 cases. *Injury* 2003; **34** Suppl 2: B55-B62. [DOI: 10.1016/j.injury.2003.09.025]
 16. Sawaguchi T, Takeuchi R, Nakamura R, Yonekura A, Akiyama T, Kerstan M, Goldhahn S. Outcome after treatment of osteoarthritis with open-wedge high-tibial osteotomy with a plate – 2-year results of a Japanese cohort study. *J Orthop Surg (Hong Kong)* 2020; **28**: 2309499019887997. [DOI: 10.1177/2309499019887997]
 17. Koshino T. The treatment of spontaneous osteonecrosis of the knee by high tibial osteotomy with and without bone-grafting or drilling of the lesion. *J Bone Joint Surg Am* 1982; **64**: 47-58.
 18. Brittberg M, Aglietti P, Gambardella R, Hangody L, Hauselmann HJ, Jakob RP, Levine D, Lohmander S, Mandelbaum BR, Petersen L, Staubli H-U. ICRS cartilage injury evaluation package - A: Patient part - B: Surgeons part. Münchenwiler,CH, Göteborg, S2000: 16.
 19. Brittberg M and Winalski CS. Evaluation of cartilage injuries and repair. *J Bone Joint Surg Am* 2003; **85-A** Suppl 2: 58-69 [DOI: 10.2106/00004623-200300002-00008]
 20. Takeuchi R, Ishikawa H, Aratake M, Bito H, Saito I, Kumagai K, Hayashi R, Sasaki Y, Akamatsu Y, Ishikawa H, Amakado E, Aota Y, Saito T. Medial opening wedge high tibial osteotomy with early full weight bearing. *Arthroscopy* 2009; **25**: 46-53. [DOI: 10.1007/s00167-008-0698-4]
 21. Goldhahn S, Takeuchi R, Nakamura N, Nakamura R, Sawaguchi T. Responsiveness of the Knee Injury and Osteoarthritis Outcome Score (KOOS) and the Oxford Knee Score (OKS) in Japanese patients with high tibial osteotomy. *J Orthop Sci.* 2017. **22**: 862-867. [DOI: 10.1016/j.jos.2017.04.013]
 22. Takeuchi R, Ishikawa H, Kumagai K, Yamaguchi Y, Chiba N, Akamatsu Y, Saito T. Fractures around the lateral cortical hinge after a medial opening-wedge high tibial osteotomy: a new classification of lateral hinge fracture. *Arthroscopy* 2012; **28**: 85-94. [DOI: 10.1016/j.arthro.2011.06.034]
 23. Nakamura N, Takeuchi R, Sawaguchi T, Ishikawa H, Saito T, Goldhahn S. Cross-cultural adaptation and validation of the Japanese Knee Injury and Osteoarthritis Outcome Score (KOOS). *J Orthop Sci* 2011; **16**: 516-523. [DOI: 10.1007/s00776-011-0112-9]
 24. Takeuchi R, Sawaguchi T, Nakamura N, Ishikawa H, Saito T, Goldhahn S. Cross-cultural adaptation and validation of the Oxford 12-item knee score in Japanese. *Arch Orthop Trauma Surg* 2010; **131**: 247-254. [DOI: 10.1007/s00402-010-1185-1]
 25. Gandek B, Ware JE, Jr., Aaronson NK, Alonso J, Apolone G, Bjorner J, Brazier J, Bullinger M, Fukuhara S, Kaasa S, Leplège A, Sullivan M. Tests of data quality, scaling assumptions, and reliability of the SF-36 in eleven countries: results from the IQOLA Project. International Quality of Life Assessment. *J Clin Epidemiol* 1998; **51**: 1149-1158. [DOI: 10.1016/s0895-4356(98)00106-1]
 26. Fukuhara S, Bito S, Green J, Hsiao A, Kurokawa K. Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. *J Clin Epidemiol* 1998; **51**: 1037-1044. [DOI: 10.1016/s0895-4356(98)00095-x]
 27. Fukuhara S, Ware JE Jr, Kosinski M, Wasa S, Gandek B. Psychometric and clinical tests of validity of the Japanese SF-36 Health Survey. *J Clin Epidemiol* 1998; **51**: 1045-1053. [DOI: 10.1016/s0895-4356(98)00096-1]
 28. The Japanese Orthopaedic Association for the osteoarthritic knee score (JOA score). *J Jpn Orthop Assoc* 1992; **66**: 1212-1219.
 29. Kellgren JH, Jeffrey MR and Ball J. The epidemiology of chronic rheumatism. Atlas of Standard Radiographs of Arthritis 1963; Volume two: iv53.
 30. Audige L, Goldhahn S, Daigl M, Goldhahn J, Blauth M, Hanson B. How to document and report orthopedic complications in clinical studies? A proposal for standardization. *Arch Orthop Trauma Surg* 2014; **134**: 269-275. [DOI: 10.1007/s00402-011-1384-4]
 31. Moyer R, Birmingham T, Lorbergs A, Eckstein F, Wirth W, Giffin JR. Decreased medial compartment loading and increased medial femorotibial articular cartilage thickness 12 months after limb realignment surgery. *Osteoarthritis Cartilage* 2018; **26**: S279-S280. [DOI: 10.1016/j.joca.2018.02.565]
 32. Birmingham TB, Moyer R, Leitch K, Chesworth B, Bryant B, Willits K, Litchfield R, Fowler PJ, Giffin JR. Changes in biomechanical risk factors for knee osteoarthritis and their association with 5-year clinically important improvement after limb realignment surgery. *Osteoarthritis Cartilage* 2017; **25**: 1999-2006. [DOI: 10.1016/j.joca.2017.08.017]
 33. Kumagai K, Akamatsu Y, Kobayashi H, Kusayama Y, Koshino T, Saito T. Factors affecting cartilage repair after medial opening-wedge high tibial osteotomy. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 779-784. [DOI: 10.1007/s00167-016-4096-z]
 34. Kim KI, Seo MC, Song SJ, Bae DK, Kim DH, Lee SH. Change of Chondral Lesions and Predictive Factors After Medial Open-Wedge High Tibial Osteotomy With a Locked Plate System. *Am J Sports Med* 2017; **45**: 1615-1621. [DOI: 10.1177/0363546517694864]
 35. Goshima K, Sawaguchi T, Sakagoshi D, Shigemoto K, Hatsuchi Y, Akahane M. Age does not affect the clinical and radiological outcomes after open-wedge high tibial osteotomy. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 918-923. [DOI: 10.1007/s00167-015-3847-6]
 36. Robinson WH, Lepus CM, Wang Q, Raghu H, Mao R, Lindstrom TM, Sokolove J. Low-grade inflammation as a key mediator of the pathogenesis of osteoarthritis. *Nat Rev Rheumatol* 2016; **12**: 580-592. [DOI: 10.1038/nrrheum.2016.136]
 37. Wang Y, Teichtahl AJ, Abram F, Hussain SM, Pelletier JP, Cicuttini FM, Martel-Pelletier J. Knee pain as a predictor of structural progression over 4 years: data from the Osteoarthritis Initiative, a prospective cohort study. *Arthritis Res Ther* 2018; **20**: 250. [DOI: 10.1186/s13075-018-1751-4]
 38. Henriksen M, Creaby MW, Lund H, Juhl C, Christensen R. Is there a causal link between knee loading and knee osteoarthritis progression? A systematic review and meta-analysis of cohort studies and randomised trials. *BMJ Open* 2014; **4**: e005368. 2014-07-18. [DOI: 10.1136/bmjopen-2014-005368]
 39. Takeuchi R, Aratake M, Bito H, Saito I, Kumagai K, Hayashi R, Sasaki Y, Akamatsu Y, Ishikawa H, Amakado E, Aota Y, Saito T. Clinical results and radiographical evaluation of opening wedge high tibial osteotomy for spontaneous osteonecrosis of the knee.

- Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 361-368. [DOI: 10.1007/s00167-008-0698-4]
40. Takemae T, Omori G, Nishino K, Terajima K, Koga Y, Endo N. Three-dimensional knee motion before and after high tibial osteotomy for medial knee osteoarthritis. *J Orthop Sci* 2006; **11**: 601-606. [DOI: 10.1007/s00776-006-1066-1]
 41. Leitch KM, Birmingham TB, Dunning CE, Griffin JR. Medial opening wedge high tibial osteotomy alters knee moments in multiple planes during walking and stair ascent. *Gait Posture* 2015; **42**: 165-171. [DOI: 10.1016/j.gaitpost.2015.05.005]
 42. Jung WH, Takeuchi R, Chun CW, Lee JS, Ha, JH, Kim JH, Jeong JH. Second-look arthroscopic assessment of cartilage regeneration after medial opening-wedge high tibial osteotomy. *Arthroscopy* 2014; **30**: 72-79. [DOI: 10.1016/j.arthro.2013.10.008]
 43. McNamara I, Birmingham TB, Fowler PJ, Griffin JR. High tibial osteotomy: evolution of research and clinical applications--a Canadian experience. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 23-31. [DOI: 10.1007/s00167-012-2218-9]
 44. Smith WB II, Steinberg J, Scholtes S, McNamara IR. Medial compartment knee osteoarthritis: age-stratified cost-effectiveness of total knee arthroplasty, unicompartmental knee arthroplasty, and high tibial osteotomy. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 924-933. [DOI: 10.1007/s00167-015-3821-3]
 45. Konopka JF, Gomoll AH, Thornhill TS, Katz JN, Losina E. The cost-effectiveness of surgical treatment of medial unicompartmental knee osteoarthritis in younger patients: a computer model-based evaluation. *J Bone Joint Surg Am* 2015; **97**: 807-817. [DOI: 10.2106/JBJS.N.00925]
 46. Ekeland A, Nerhus TK, Dimmen S, Thornes E, Heir S. Good functional results following high tibial opening-wedge osteotomy of knees with medial osteoarthritis: A prospective study with a mean of 8.3 years of follow-up. *Knee* 2017; **24**: 380-389. 2017/01/14. [DOI: 10.2106/JBJS.N.00925]
 47. Song KY, Koh IJ, Kim MS, Choi NY, Jeong JH, In Y. Early experience of lateral hinge fracture during medial opening-wedge high tibial osteotomy: incidence and clinical outcomes. *Arch Orthop Trauma Surg* 2020; **140**: 161-169. [DOI: 10.1007/s00402-019-03237-0]

ADDITIONAL FILES

Additional file 1. Corresponding study results at 5 years for the conservative group: Functional, radiological and patient-reported outcomes are shown for the conservative group between baseline and 5 years.

Table 1 Summary of the Knee Osteoarthritis Outcome Score (KOOS) at baseline, and at follow-ups after 2 years and 5 years (sensitivity analysis on conservative patients with data available for both time points).

Visit	KOOS subscales				
	Pain	Symptoms	ADL	Sports	QOL
n	18	18	18	18	18
Baseline					
Mean (sd)	52.0 (21.6)	62.5 (19.0)	73.0 (18.9)	34.4 (24.7)	40.6 (20.7)
Min; Max	19.4; 97.2	25.0; 85.7	32.4; 100.0	5.0; 90.0	6.3; 81.3
2 years					
n	18	18	18	18	18
Mean (sd)	81.3 (16.5)	84.9 (13.2)	90.0 (11.1)	70.8 (26.4)	68.1 (15.4)
Min; Max	36.1; 100.0	50.0; 100.0	61.8; 100.0	5.0; 100.0	37.5; 93.8
5 years					
n	18	18	18	18	18
Mean (sd)	79.9 (18.4)	81.5 (19.5)	88.6 (16.4)	75.3 (22.1)	73.3 (16.9)
Min; Max	27.8; 97.2	28.6; 100.0	30.9; 100.0	5.0; 100.0	37.5; 93.8

ADL: activities of daily living; KOOS: Knee Injury and Osteoarthritis Outcome Score; QOL: quality of life. Highest score = 100; lowest score = 0.

Table 2a Mean change from baseline in the subscales of Knee Osteoarthritis Outcome Score (KOOS) at 5 years (enrolled conservative patients)

Outcome	Follow-up	Mean (95% CI)	Mean change from baseline (95% CI)	P value*
KOOS Pain	Baseline	52.8 (46.2;59.3)	-	-
	5 years	78.2 (71.4;85.0)	25.4 (14.5;36.4)	<.001
KOOS Symptoms	Baseline	59.6 (52.4;66.8)	-	-
	5 years	76.8 (70.0;83.6)	17.2 (6.6;27.8)	<.001
KOOS ADL	Baseline	71.8 (65.9;77.7)	-	-
	5 years	86.2 (80.5;91.9)	14.4 (5.8;23.0)	<.001
KOOS Sport	Baseline	29.8 (21.9;37.8)	-	-
	5 years	69.9 (58.5;81.3)	40.1 (23.7;56.5)	<.001
KOOS QOL	Baseline	34.2 (27.9;40.5)	-	-
	5 years	70.4 (61.8;78.9)	36.2 (23.1;49.3)	<.001

*P value for within-group change from baseline, mixed effects model for repeated measures with unstructured covariance. Means, mean change from baseline and P values were derived from a mixed effects model for repeated measures with unstructured covariance. P values and confidence intervals for change from baseline were adjusted for multiple testing at several time points with simulation-based approach.

Table 2b Mean change from baseline to 5 years in Oxford 12-item Knee Score (OKS), The Japanese Orthopaedic Association (JOA) knee score, range of motion (ROM) and the SF-36 component summaries by follow-up (enrolled conservative patients).

Outcome	Follow-up	Mean (95% CI)	Mean change from baseline (95% CI)	P value*
OKS	Baseline	30.3 (27.4;33.2)	-	-
	5 years	19.4 (16.3;22.6)	-10.9 (-15.6;-6.1)	<.001
JOA	Baseline	69.7 (64.4;74.9)	-	-
	5 years	87.0 (82.4;91.5)	17.3 (9.3;25.3)	<.001
Absolute ROM	Baseline	130.1 (124.4;135.7)	-	-
	5 years	136.3 (131.3;141.3)	6.2 (-1.9;14.4)	0.17
Relative ROM	Baseline	93.7 (90.1;97.3)	-	-
	5 years	98.6 (96.2;101.0)	4.9 (-0.3;10.0)	0.07
PCS	Baseline	27.7 (22.4;33.0)	-	-
	5 years	44.7 (38.6;50.9)	17.0 (7.2;26.9)	<.001
MCS	Baseline	51.4 (48.1;54.8)	-	-
	5 years	51.1 (47.3;55.0)	-0.3 (-5.4;4.8)	1

OKS: Oxford 12-item Knee Score (OKS), JOA: The Japanese Orthopaedic Association knee score, ROM: range of motion, PCS: Physical Component Summary, MCS: Mental Component Summary. *P value for within-group change from baseline to follow-ups, mixed effects model for repeated measures with unstructured covariance. Means, mean change from baseline and P values were derived from a mixed effects model for repeated measures with unstructured covariance. P values and confidence intervals for change from baseline were adjusted for multiple testing at several time points with simulation-based approach.

Table 3 Grades of osteoarthritis (OA) at baseline and 5 years (enrolled conservative patients).

Characteristics	Baseline, n (%)	5 years, n (%)
Grade OA Kellgren-Lawrence*	30	18
No OA	0 (0.0)	0 (0.0)
Grade 1	14 (46.7)	7 (38.9)
Grade 2	8 (26.7)	3 (16.7)
Grade 3	5 (16.7)	6 (33.3)
Grade 4	3 (10.0)	2 (11.1)
Not measurable	0 (0.0)	0 (0.0)

*knee full extension ap -standing

Additional file 2. Prognostic factors with significant influence on the KOOS subscale scores after 5 years in patients treated with OWHTO. This univariable regression analyses show that different prognostic factors had a significant influence on the five KOOS subscale scores at 5 years.

KOOS Pain

1. Per 12 months of increase in OA history (expressed as months of OA suffered) the mean (95% CI) score decreased by 0.9 (0.3; 1.6) points, $P = 0.006$;
2. Per unit increase of BMI at baseline, the mean (95% CI) score decreased by 1.0 (0.0; 2.0) point ($P = 0.041$);
3. Per ten points increase of CSS at baseline, the mean (95% CI) score increased by 2.1 (0.0; 4.2) points, $P = 0.047$;
4. Higher grade of Kellgren-Lawrence classification was associated with a decreased score, $P < 0.001$ in comparison to baseline OA status of Kellgren-Lawrence grade 1.

KOOS Symptoms

1. Per ten points increase of KOOS Symptoms at baseline, the mean (95% CI) score increased by 2.2 (0.8; 3.6) points, $P = 0.002$;
2. Per unit increase of BMI at baseline, each additional unit was associated with a decrease of mean (95% CI) by 1.2 (0.2; 2.2) points ($P = 0.018$);
3. Per ten points increase of VAS score for general pain at baseline, the mean (95% CI) score decreased by 1.5 (0.4; 2.5) points, $P = 0.008$;
4. Per ten points increase of CSS at baseline, the mean (95% CI) score increased by 3.3 (1.3; 5.3) points, $P = 0.002$;
5. Higher grade of Kellgren-Lawrence classification was associated with a decreased score, $P = 0.005$, in comparison to baseline OA status of Kellgren-Lawrence grade 1.

KOOS ADL

1. Per ten points increase of KOOS ADL at baseline, the mean (95% CI) score increased by 2.1 (0.8; 3.5) points, $P = 0.002$;
2. Per ten years increase of age at baseline, the mean (95% CI) decreased by 4.5 (1.9; 7.0) points ($P < 0.001$);
3. Per 12 months increase in OA history, the mean (95% CI) score decreased by 0.8 (0.3; 1.4) points, $P = 0.003$;
4. Per unit increase of BMI at baseline, the mean (95% CI) score decreased by 0.9 (0.1; 1.8) points ($P = 0.023$);
5. Per ten points increase of general VAS at baseline, the mean (95% CI) score decreased by 1.0 (0.2; 1.9) points, $P = 0.021$;
6. Higher grade of Kellgren-Lawrence classification was associated with a decreased score, $P < 0.001$, in comparison to baseline OA status of Kellgren-Lawrence grade 1.

KOOS Sport

1. Per ten years increase of age at baseline, the mean (95% CI) decreased by 8.7 (3.5; 13.9) points ($P = 0.001$);
2. Per unit increase of BMI at baseline, the mean (95% CI) score decreased by 2.0 (0.3; 3.6) points ($P = 0.018$);
3. Per ten points increase of VAS general pain score at baseline the mean (95% CI) score decreased by 2.0 (0.2; 3.8) points, $P = 0.027$;
4. Per ten points increase of CSS at baseline, the mean (95% CI) score increased by 4.5 (0.8; 8.1) points, $P = 0.017$;
5. Higher grade of Kellgren-Lawrence classification was associated with a decreased score, $P < 0.001$, in comparison to baseline OA status of Kellgren-Lawrence grade 1.

KOOS QOL

1. Per ten points increase of VAS at baseline, the mean (95% CI) score decreased by 1.8 (0.5; 3.2) points, $P = 0.006$;
2. Higher grade of Kellgren-Lawrence classification was associated with a decreased score, $P < 0.022$, in comparison to baseline OA status of Kellgren-Lawrence grade 1.