Long-Term Clinical Outcomes and Implant Survivorship of 151 Total Ankle Arthroplasties Using the HINTEGRA Prosthesis

A Minimum 10-Year Follow-up

Yeo Kwon Yoon, MD, Kwang Hwan Park, MD, PhD, Jae Han Park, MD, Wonwoo Lee, MD, Seung Hwan Han, MD, PhD, and Jin Woo Lee, MD, PhD

Investigation performed at the Department of Orthopaedic Surgery, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea

Background: Few studies have investigated long-term clinical outcomes of a mobile-bearing total ankle arthroplasty (TAA) system. This study analyzed long-term outcomes of TAA using the HINTEGRA prosthesis at a single, non-developer center.

Methods: Primary TAAs were performed on 213 ankles in 194 patients, and 151 consecutive ankles [71%] in 136 patients with a minimum follow-up of 10 years after the primary TAA were included in this study. Clinical results were assessed using a visual analog scale (VAS) pain score, the American Orthopaedic Foot & Ankle Society (AOFAS) Ankle-Hindfoot Scale score, the Ankle Osteoarthritis Scale (AOS) pain and disability subscores, and ankle range of motion. Prosthesis survivorship, reoperations, and risk factors were also evaluated.

Results: The mean follow-up was 135.5 months (range, 120.0 to 204.0 months). All clinical scores and ankle range of motion improved significantly from preoperatively to 2 years, 4 to 6 years, and ≥10 years after TAA ($p < 0.001$). A total of 43 ankles (28.5%) required revision procedures, with the most common reason being periprosthetic osteolysis (32 ankles [21.2%]). The overall implant survivorship was 93.5% in Kaplan-Meier survival analysis at the mean follow-up of 11.3 years after the TAA.

Conclusions: TAA using the HINTEGRA prosthesis with careful follow-up observation and appropriate adjunct procedures for the treatment of end-stage ankle arthritis produced satisfactory clinical results, which were maintained at a follow-up of ≥10 years, and resulted in 93.5% of implant survivorship.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Patients with end-stage ankle arthritis have severe pain, limited physical function, and substantial reductions in general health and quality of life[1]. Traditionally, ankle arthrodesis was considered the surgical standard for treating end-stage ankle arthritis whose symptoms are inadequately relieved with conservative management. Despite the predictable results of arthrodesis, concerns have been raised with regard to loss of ankle motion, decreased gait efficiency, and the development of arthritic changes in adjacent joints[2].

Total ankle arthroplasty (TAA) has emerged as a viable alternative to ankle arthrodesis. Recent improvements in implant design and surgical technique have produced encouraging outcomes[2,3]. Moreover, in several recent studies, authors have suggested that TAA can be superior to ankle arthrodesis in terms of patient function[4-6]. The HINTEGRA total ankle replacement system (Newdeal/Integra) is a 3-component, unconstrained system[7]. The reported outcomes of the mobile-bearing HINTEGRA prosthesis have been favorable. In 722 TAAs with a mean follow-up of 6.3 years, the implant developers reported survivorship rates of 94% after 5 years and 84% after 10 years[8]. Despite satisfactory survivorship rates, reports of long-term functional results have been limited, and many previous studies had the implant developers as authors.

Therefore, the aim of the present study was to report long-term clinical outcomes and implant survivorship over a minimum follow-up period of 10 years in 151 consecutive ankles treated with TAA with the HINTEGRA prosthesis.

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJS/H114).

TABLE I Concomitant Procedures

Procedure	Ankles* (N = 151)
Medial deltoid release	61 (40.4%)
Heel cord lengthening	46 (30.5%)
Lateral plication	13 (8.6%)
Calcaneal lateral closing-wedge osteotomy	8 (5.3%)
First metatarsal dorsiflexion osteotomy	8 (5.3%)
Simultaneous bone grafting for bone defect	4 (2.6%)
Fibular lengthening osteotomy	2 (1.3%)
Flexor digitorum longus tendon transfer	1 (0.7%)
Fixation of medial malleolus	1 (0.7%)
Posterior tibial tendon repair	1 (0.7%)
Deltoid ligament reconstruction	1 (0.7%)

*The values are given as the number of ankles, with the percentage in parentheses.

Materials and Methods

The institutional review board of our hospital approved this study (approval number: 4-2021-1369), and informed consent was obtained from each patient.

Between September 2004 and October 2011, 213 consecutive primary TAAs were performed on 194 patients. The HINTEGRA third-generation total ankle system, a 3-component, mobile-bearing, uncemented implant, was used in all cases. The senior author (J.W.L.) performed all procedures at a single center.

The indication for TAA was painful end-stage ankle arthritis refractory to conservative treatment. To be included in the final cohort, patients must have had regular follow-up for at least 10 years. We excluded patients with a history of osteonecrosis of the talus, septic arthritis, inadequate soft tissue or bone stock, a neuromuscular disorder, Charcot neuroarthropathy, poor vascularity, or previous ankle arthrodesis. Patients lost to follow-up for >2 years were also excluded. After exclusions, 151 ankles (136 patients) were included in the final analysis (see Appendix Figure 1).

TAA was performed in a standardized manner introduced by the implant developers[7]. Appropriate concomitant procedures were performed during TAA, according to previously reported treatment algorithms for malalignment and instability[9-11]. The standard protocol required wearing a below-the-knee cast for 4 weeks after the surgical procedure, with patients permitted to return to full-weight-bearing as tolerated. However, if realignment osteotomy was performed, the duration of immobilization and non-weight-bearing was potentially prolonged. Range of motion and muscle-strengthening exercises were allowed after cast removal. Data were collected with regard to concomitant and subsequent procedures. Concomitant procedures were defined as any additional procedure performed during the primary TAA and are summarized in Table I. Subsequent procedures were defined as additional procedures performed after the initial surgical procedure and not involving the prosthetic components.

Clinical Evaluation

The patients' baseline demographic data such as age, sex, body mass index, and medical history were evaluated on the basis of the patient descriptions in the electronic medical records.

The visual analog scale (VAS) pain score, Ankle Osteoarthritis Scale (AOS) pain and disability subscores[12], American Orthopaedic Foot & Ankle Society (AOFAS) Ankle-Hindfoot Scale score[13], and ankle range of motion were assessed preoperatively and at 2 years postoperatively to evaluate short-term functional outcomes, 4 to 6 years postoperatively to evaluate intermediate-term functional outcomes, and ≥10 years postoperatively to evaluate long-term functional outcomes. If scores were measured multiple times during the period of 4 to 6 years or the period of ≥10 years, the last score during the period was used. Ankle range of motion was measured using a goniometer along the lateral border of the leg and foot with the ankle in maximal dorsiflexion and plantar flexion. Two independent observers blinded to the intent of this study (J.H.P. and K.H.P.) conducted the clinical scoring.

Revision was defined as a surgical procedure involving any prosthetic component, including insert exchange[14]. Major revision with prosthesis failure was defined as the exchange or removal of any metal component. Minor revision was defined as any surgical procedure involving exchange of the polyethylene inlay. The period from TAA to prosthesis failure was recorded and used in survival analysis.

Radiographic Evaluation

All patients underwent standardized weight-bearing anteroposterior and lateral radiographs of the ankle preoperatively. Fluoroscopy-assisted standing anteroposterior and lateral radiographs were obtained to evaluate the implant position at 6 weeks postoperatively and at every follow-up visit thereafter. Computed tomography (CT) with metal artifact subtraction was performed in all patients during the follow-up period: every 3 years for patients without evidence of osteolysis on radiographs and more frequently for patients with suspected progressive osteolysis. All radiographic data were evaluated by 2 authors (S.H.H. and Y.K.Y.). They performed measurements twice, and the mean of the values was recorded. The preoperative coronal tibiotalar angle was measured on the standing anteroposterior radiograph and was defined as the angle between the anatomic axis of the tibia and a line perpendicular to the articular surface of the talus[15]. The preoperative anterior distal tibial angle was measured on the standing lateral radiograph and was defined as the angle between the anatomic axis of the tibia and a line connecting the most distal points on the anterior and posterior portions of the tibial articular surface. Postoperative alignment and component migration were assessed using α, β, and γ angles (Figs. 1-A through Figs. 1-D)[7]. The development of osteolytic cysts or heterotopic ossification was recorded. Osteolysis was

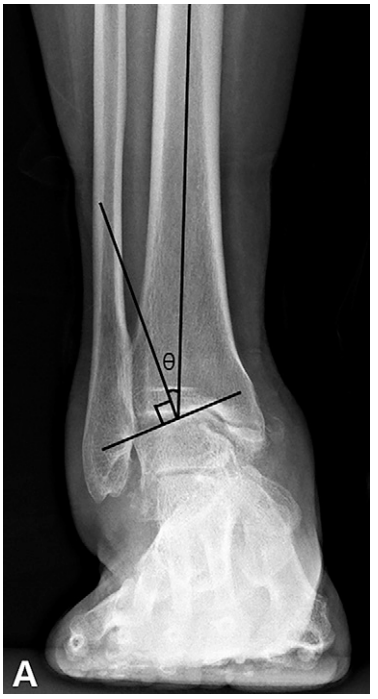
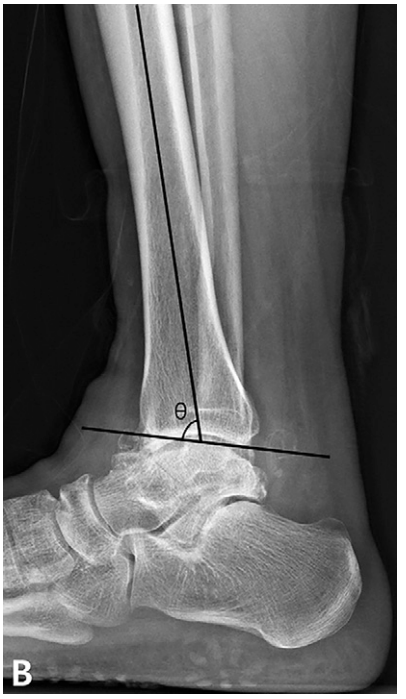


Fig. 1-A



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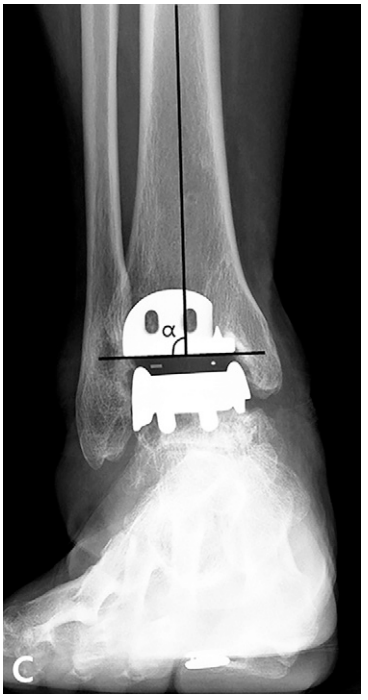

Fig. 1-C

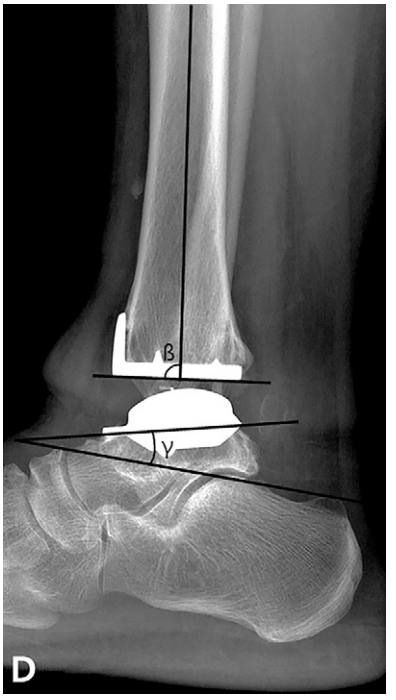

Fig. 1-D

Fig. 1-A A standing anteroposterior radiograph showing the preoperative tibiotalar angle, defined as the angle between the anatomic axis of the tibia and a line perpendicular to the articular surface of the talus. **Fig. 1-B** A standing lateral radiograph showing the preoperative anterior distal tibial angle, defined as the angle between the anatomic axis of the tibia and a line connecting the most distal points on the anterior and posterior tibial articular surface. **Fig. 1-C** A standing anteroposterior radiograph showing the α angle, defined as the angle between the anatomic axis of the tibia and the articulating surface of the tibial component. **Fig. 1-D** A standing lateral radiograph showing the β angle, defined as the angle between the longitudinal axis of the tibia and the articulating surface of the tibial component, and the γ angle, defined as the angle between a line drawn through the anterior shield and the posterior edge of the talar component and a line drawn between the dorsal aspect of the talonavicular joint and the calcaneal tubercle.

defined as a demarcated hypodense lesion >2 mm in width on CT images[16].

Statistical Analysis

The Shapiro-Wilk test was used to assess the normality of the distribution of each variable. Changes in clinical scores and ankle range of motion over time were evaluated using repeated-measures analysis of variance at 4 time points: preoperatively and at 2 years, 4 to 6 years, and ≥10 years (the latest follow-up) after the surgical procedure. Post hoc tests were performed using the Bonferroni correction to identify significantly different time points. The probability of prosthesis failure was estimated using Kaplan-Meier analysis. To analyze individual factors associated with prosthesis failure and revision surgery, the chi-square test or Fisher exact test was used for categorical variables and the independent-sample t test or Mann-Whitney U test was used for continuous variables. Logistic regression analysis was used to assess possible associations of selected variables with prosthesis failure and revision. Significant independent variables in bivariate analysis were eligible for entry into logistic regression models. Statistical analyses were performed using SPSS version 26.0 (IBM). Significance was set at $p < 0.05$.

Source of Funding

This study had no external source of funding.

Results

Patient demographic data are presented in Table II. The study included 79 ankles in female patients and 72 ankles in male patients, with a median patient age of 65.0 years (interquartile range: 56.0, 69.0 years [range, 33 to 81 years]). The etiology of arthritis was as follows: 75 ankles (49.7%) had posttraumatic osteoarthritis, 63 ankles (41.7%) had degenerative osteoarthritis, and 13 ankles (8.6%) had inflammatory arthritis. The mean follow-up period was 135.5 months (range, 120 to 204 months).

Clinical Outcomes

Clinical outcomes over time are summarized in Figure 2. All scores and ankle motion improved significantly from preoperatively to all follow-up periods (all $p < 0.001$). All clinical scores had a tendency to decline slightly as the postoperative follow-up period progressed. However, there were no differences in VAS pain score ($p = 0.500$) or AOS pain score ($p = 0.325$) between the intermediate-term and long-term follow-up periods. Although the AOS disability score remained better than the preoperative score at all follow-up times, the score progressively worsened at each time period.

Radiographic Outcomes

Postoperative alignment results of the components are shown in Table III. The mean α, β, and γ angles were not significantly different between 6 weeks postoperatively and the latest follow-up. There were 146 osteolytic cysts observed in 89 ankles (58.9%): 83 tibial cysts (56.8%), 57 talar cysts (39.0%), and 6 fibular cysts (4.1%). Heterotopic ossification was detected in 59 ankles (39.1%).

Subsequent Procedures

Subsequent procedures are summarized in Table IV. The most common reason for a subsequent procedure was gutter pain. Arthroscopic or open gutter debridement was performed in 9 ankles (6.0%). Curettage and bone grafting for a progressive osteolytic cyst of the fibula or tip of the medial malleolus were required in 8 ankles (5.3%).

Revision and Prosthesis Failure

Revision surgery was performed in 43 ankles (28.5%): 9 major revisions (6.0%) and 34 minor revisions (22.5%). The reasons for revision surgery are shown in Table V, and the types of procedures are summarized in Table VI. The most common reason for revision surgery was progressive periprosthetic osteolysis (32 ankles [21.2%]). Seven ankles (4.6%) with aseptic loosening or component subsidence underwent tibial component revision (4 ankles [2.6%]) or conversion to tibiotalocalcaneal arthrodesis (3 ankles [2.0%]). For the other 25 ankles (16.6%) without loosening or subsidence of a component, curettage of an osteolytic cyst, autogenous iliac cancellous bone grafting, and polyethylene inlay exchange were performed. There were 4 ankles (2.6%) with asymmetric inlay wear and 4 ankles (2.6%) with instability involving dislocation or subluxation of the inlay. For these cases, lateral plication with inlay exchange was performed in 4 ankles (2.6%), valgus correction with inlay exchange was performed in 2

TABLE II Patient Demographic and Radiographic Characteristics

Characteristic	Value
No. of ankles	151
No. of patients	136
Age at the time of the operation* *(yr)*	65.0 (56.0, 69.0)
Sex†	
Female	79 (52.3%)
Male	72 (47.7%)
Ankle side†	
Right	85 (56.3%)
Left	66 (43.7%)
Body mass index‡ *(kg/m²)*	25.3 (18.6 to 35.3)
Etiology†	
Posttraumatic osteoarthritis	75 (49.7%)
Degenerative osteoarthritis	63 (41.7%)
Inflammatory arthritis	13 (8.6%)
Preoperative radiographic angle‡ *(deg)*	
Coronal tibiotalar	7.4 (−31.8 to 29.7§)
Anterior distal tibial	74.8 (52.5 to 89.9)
Follow-up period‡ *(mo)*	135.5 (120.0 to 204.0)

*The values are given as the median, with the interquartile range in parentheses. †The values are given as the number of ankles, with the percentage in parentheses. ‡The values are given as the mean, with the range in parentheses. §Positive values are considered varus and negative values are considered valgus.

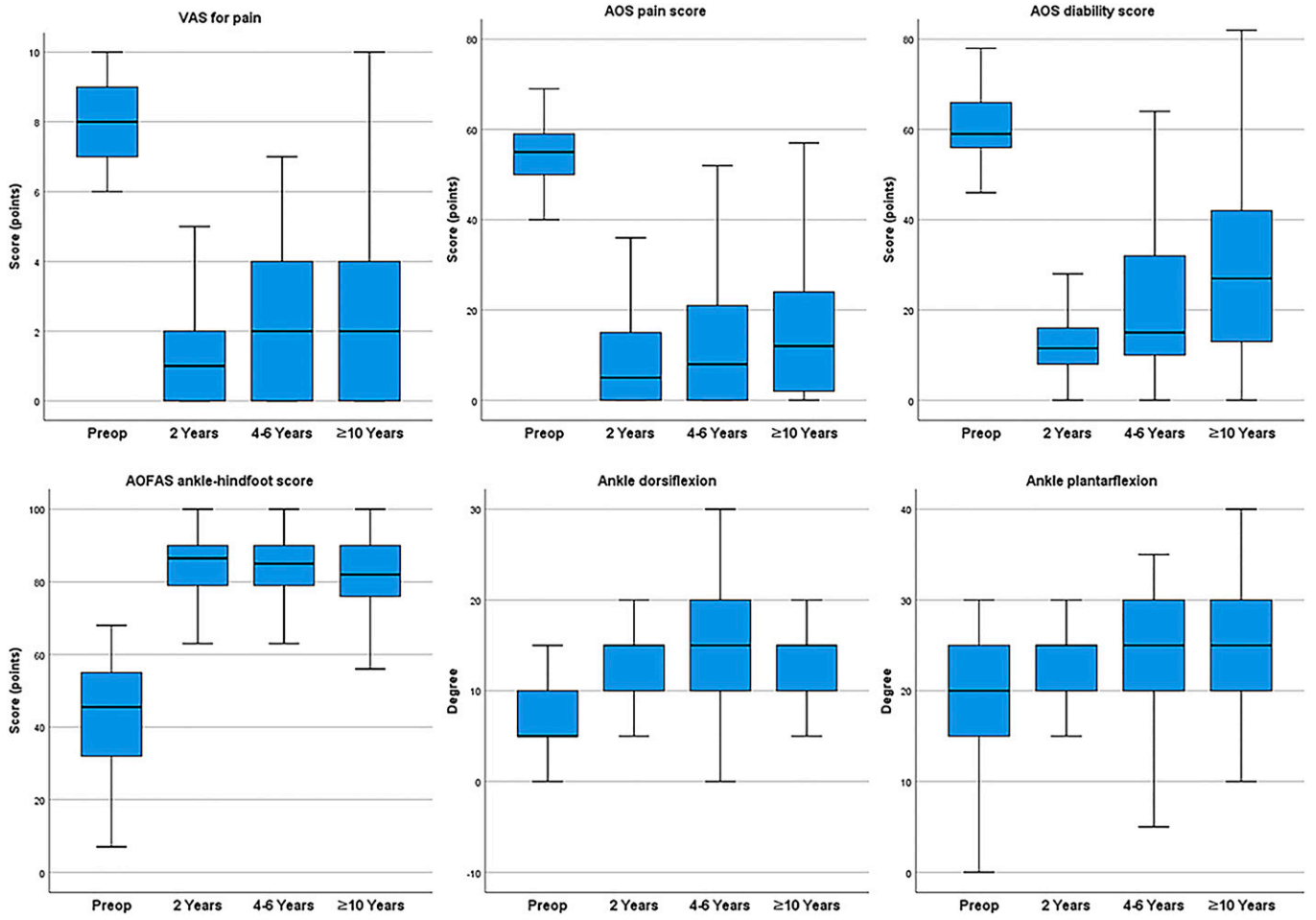

Fig. 2
Clinical outcomes throughout the follow-up period.

ankles (1.3%), and solitary inlay exchange was performed in 2 ankles (1.3%). There were 2 cases of deep infection. One of these patients was treated with 2-stage conversion to a tibiotalocalcaneal arthrodesis. The other patient underwent implant removal and cementoplasty; we recommended 2-stage conversion to tibiotalocalcaneal arthrodesis, which the patient declined. One case of inlay breakage was successfully treated with inlay exchange.

The mean interval from primary TAA to revision surgery was 68.2 months (range, 1.0 to 140.0 months). No prosthesis failure was observed after minor revision. The probability of prosthesis survivorship when only metal component revision was considered failure, estimated by Kaplan-Meier analysis, was 93.5% at a mean follow-up of 135.5 months (Fig. 3). With revision of any prosthetic component including the polyethylene inlay as the end point, the survival rate at a mean of 11.3 years was 75.2%.

TABLE III Component Alignment of the HINTEGRA TAA System

Component Alignment *(deg)*	6 Weeks Postoperatively*	Latest Follow-up*	P Value
α angle	91.5 ± 2.1	91.8 ± 2.1	0.133
β angle	86.8 ± 2.4	86.7 ± 2.3	0.211
γ angle	12.0 ± 4.8	12.2 ± 4.9	0.150

*The values are given as the mean and the standard deviation.

Factors Associated with Prosthesis Failure and Revision

Comparative analyses were performed to identify risk factors for prosthesis failure. A number of variables, including baseline demographic and radiographic parameters, were evaluated. No individual factor was significantly associated with prosthesis failure (Table VII).

With regard to revision surgery, the only significant difference between patients who had or had not undergone revision surgery was chronic treatment with oral anticoagulation ($p = 0.003$) (Table VII). Univariate logistic regression analysis confirmed chronic therapeutic oral anticoagulation as a risk factor for revision surgery, with an odds ratio (OR) of 3.168 (95% confidence interval [CI], 1.457 to 6.886; $p = 0.004$) (Table VIII).

Discussion

This study is one of the largest series of TAAs that was conducted by researchers independent of the TAA developers and evaluated both functional outcomes and implant

TABLE IV Subsequent Procedures

Procedure	Ankles* (N = 151)
Gutter debridement	9 (6.0%)
Bone grafting for osteolytic cyst of fibula or tip of medial malleolus	8 (5.3%)
Excision of heterotopic ossification	2 (1.3%)
Heel cord lengthening	1 (0.7%)

*The values are given as the number of ankles, with the percentage in parentheses.

survivorship during long-term follow-up. We found that the HINTEGRA mobile-bearing TAA system significantly improved pain and function not only during short-term and intermediate-term follow-up but also for follow-up of ≥10 years, with 93.5% implant survivorship. Moreover, the present study also suggests that careful observation by radiographic follow-up and appropriate minor revision procedures, especially for periprosthetic osteolysis, may be helpful for preventing prosthesis failure.

With regard to functional outcomes, there were significant improvements from baseline for all parameters throughout the follow-up period. Yang et al.[17] followed 210 ankles that had undergone primary TAA with the HINTEGRA total ankle replacement and had a mean follow-up of 6.4 years. In that study, the median score (and interquartile range) at the last follow-up was 2.0 (0, 3.0) for the VAS, 86.0 (79.0, 96.5) for the AOFAS Ankle-Hindfoot Scale, 15.6 (5.5, 32.8) for AOS pain, and 27.7 (15.5, 42.2) for AOS disability, with significant improvements for all. In their series of 50 primary HINTEGRA total ankle replacements with a mean follow-up of 3.8 years, Deleu et al.[18] found a mean AOFAS score of 83.8 at the latest follow-up. Our results are comparable with the results of these reports, as well as those of other studies with varying prosthesis designs and follow-up periods[19-24]. Thus, positive results after TAAs appear to be maintained in the long term, suggesting that TAA is a suitable option for end-stage ankle arthritis in relatively young patients.

It is widely accepted that attaining neutral alignment and stability are fundamental to successful TAA[9]. For that reason, soft-tissue balancing and deformity correction are essential during primary TAA[9-11]. In our study, 121 ankles (80.1%) required concomitant procedures. The most common procedure was medial deltoid ligament release to correct varus imbalance. The second most common procedure was heel cord lengthening. In treating end-stage ankle arthritis, one of the noted benefits of TAA over ankle arthrodesis is the preservation of joint motion[2]. Several studies have shown positive associations between the final ankle range of motion and functional outcomes after TAA[25-27]. We performed heel cord lengthening when dorsiflexion was limited to <10° after implantation[9]. Additionally, in ankles with severe varus or valgus deformities, heel cord tightness usually aggravates the deformity. If residual stiffness with heel malalignment is present after implantation, there should be a low threshold for performing heel cord lengthening.

With regard to subsequent procedures, the most frequent procedure in this study was gutter debridement, performed in 6.0% of ankles. The reported incidence of moderate residual pain after TAA is approximately 20%[28,29]. Soft-tissue impingement is a potential cause of persistent pain after TAA without apparent complications[28]. Thus, if refractory pain persists after TAA in the absence of an obvious structural problem, operative management (mainly arthroscopic) for soft-tissue impingement may be considered[28].

The overall implant survivorship was 93.5% at a mean follow-up of 11.3 years, with the exchange or removal of a metal component as the end point. Barg et al.[8] reviewed 722 HINTEGRA total ankle replacements with a mean follow-up of 6.3 years and reported survivorship rates of 94% at 5 years and 84% at 10 years. Yang et al.[17] reported a 91.7% survivorship rate in 210 HINTEGRA total ankle replacements at a mean of 6.4

TABLE V Reasons for Revision Surgery

Reason	Ankles* (N = 151)
Progressive periprosthetic osteolysis	32 (21.2%)
Aseptic loosening	5 (3.3%)
Subsidence of metal component	2 (1.3%)
Asymmetric polyethylene inlay wear	4 (2.6%)
Instability	4 (2.6%)
Deep infection	2 (1.3%)
Polyethylene inlay breakage	1 (0.7%)

*The values are given as the number of ankles, with the percentage in parentheses.

TABLE VI Types of Revision Surgery

Procedure Type	Ankles* (N = 151)
Minor revision	34 (22.5%)
Auto-iliac bone grafting with polyethylene inlay exchange	25 (16.6%)
Lateral plication with polyethylene inlay exchange	4 (2.6%)
Polyethylene inlay exchange	3 (2.0%)
Valgus correction with polyethylene inlay exchange	2 (1.3%)
Major revision	9 (6.0%)
Tibial component revision	4 (2.6%)
Conversion to tibiotalocalcaneal arthrodesis	4 (2.6%)
Implant removal with cementoplasty	1 (0.7%)

*The values are given as the number of ankles, with the percentage in parentheses.

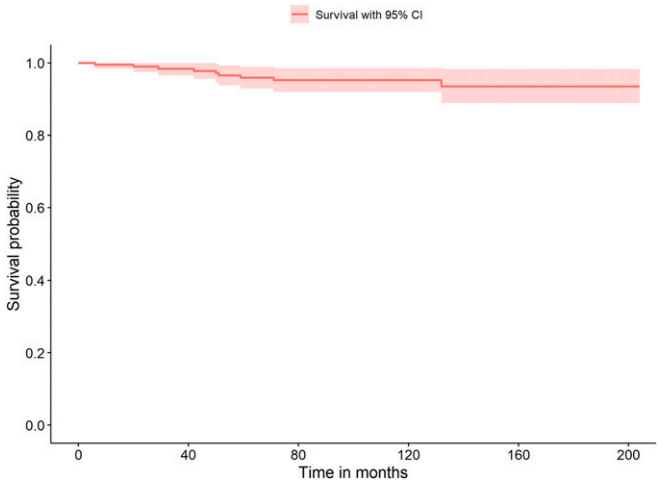

Fig. 3

Kaplan-Meier survivorship analysis of the HINTEGRA total ankle replacement, with the exchange or removal of a metallic component (implant failure) used as the end point.

years. In these 2 studies, the primary end point for survival analysis was identical to our study. Recently, Zafar et al.[30] reported survival of 75% at 5 years and 60% at 10 years of 322 HINTEGRA total ankle replacements, using the exchange of any component as the end point. The 10-year survivorship rates of approximately 80% to 90% have been reported in previous meta-analyses of TAA[31,32], with 10-year survivorship rates of individual studies ranging from 60% to 95%[19,20,22,24,33,34]. Compared with previous results, our findings are promising.

Revision surgery was performed in 43 ankles (28.5%), with 34 (22.5%) being minor revisions. A main reason for revision was progressive periprosthetic osteolysis. In managing osteolysis, 2 critical points are early detection of impending prosthesis failure and appropriate intervention before implant loosening or subsidence occurs. Annual radiographic follow-up is necessary because patients are often asymptomatic, even until immediately before loosening or subsidence[16,35,36]. In most cases, we identified progressive enlargement of cysts before prosthesis failure by obtaining CT scans at regular intervals. CT provides accurate diagnosis and measurement of osteolytic cysts and is especially useful for cysts obscured by implants on radiographs[16,35]. In our experience, aggressive management of large osteolytic cysts is required, especially for talar cysts. The absence of prosthesis failure after minor revision surgery supports this approach.

Various factors, including younger age, obesity, diabetes, preoperative deformity, and smoking, have been suggested as

TABLE VII Comparison of Demographic and Radiographic Data Between Implant Survival and Failure Groups and Between No Revision and Revision Groups

Variable	Survival (N = 142)	Failure (N = 9)	P Value	No Revision (N = 108)	Revision (N = 43)	P Value
Age* *(yr)*	64.5 (56.0, 69.0)	67.0 (53.0, 70.0)	0.403†	65.0 (57.5, 70.0)	63.0 (55.0, 67.0)	0.168†
Sex‡			0.737§			0.589#
Female	75 (52.8%)	4 (44.4%)		58 (53.7%)	21 (48.8%)	
Male	67 (47.2%)	5 (55.6%)		50 (46.3%)	22 (51.2%)	
Body mass index** *(kg/m²)*	25.3 (18.6 to 35.3)	25.0 (22.0 to 28.1)	0.418†	25.2 (18.6 to 34.8)	25.5 (20.3 to 35.3)	0.926†
Etiology‡						
Posttraumatic osteoarthritis	70 (49.3%)	5 (55.6%)	0.745§	54 (50.0%)	21 (48.8%)	0.897#
Degenerative osteoarthritis	59 (41.5%)	4 (44.4%)	1.000§	42 (38.9%)	21 (48.8%)	0.263#
Inflammatory arthritis	13 (9.2%)	0 (0%)	1.000§	12 (11.1%)	1 (2.3%)	0.111§
Bilaterality‡	30 (21.1%)	0 (0%)	0.206§	25 (23.1%)	5 (11.6%)	0.109#
Alcohol‡	62 (43.7%)	5 (55.6%)	0.511§	46 (42.6%)	21 (48.8%)	0.486#
Smoking‡	40 (28.2%)	2 (22.2%)	1.000§	29 (26.9%)	13 (30.2%)	0.691#
Diabetes mellitus‡	36 (25.4%)	4 (44.4%)	0.246§	25 (23.1%)	15 (34.9%)	0.140#
Oral anticoagulant‡	35 (24.6%)	3 (33.3%)	0.692§	20 (18.5%)	18 (41.9%)	0.003§
Oral immunosuppressant‡	14 (9.9%)	0 (0%)	1.000§	13 (12.0%)	1 (2.3%)	0.070§
Radiographic angle** *(deg)*						
Coronal tibiotalar	7.3 (−31.8 to 29.7)	10.2 (−2.0 to 26.6)	0.344†	7.9 (−15.6 to 29.7)	6.4 (−31.8 to 26.6)	0.700†
Anterior distal tibial	74.9 (52.5 to 89.9)	73.5 (61.8 to 83.1)	0.292†	75.2 (52.5 to 89.9)	73.8 (60.4 to 87.9)	0.205††

*The values are given as the median, with the interquartile range in parentheses. †Mann-Whitney U test. ‡The values are given as the number of ankles, with the percentage in parentheses. §Fisher exact test. #Chi-square test. **The values are given as the mean, with the range in parentheses. ††Student independent-sample t test.

TABLE VIII Univariate Logistic Regression Analysis of Factors Associated with Revision Surgery*

Variable	OR†	P Value
Oral anticoagulant	3.168 (1.457 to 6.886)	0.004

*Chronic oral anticoagulant use was the only risk factor associated with revision surgery in bivariate analysis (Table VII) and thus the only variable included in this regression analysis. †The value is given as the OR, with the 95% CI in parentheses.

risk factors for implant failure after TAA[8,30,37-39]. However, their role as risk factors is not supported by strong evidence. In the present study, no individual factor was significantly associated with failure, and only chronic oral anticoagulation therapy was significantly associated with an increased risk of revision surgery. Anticoagulants have been previously reported to impair bone remodeling by inducing an imbalance between osteogenesis and osteolysis[40-42]. Recently, Rocha et al.[43] reported that the oral anticoagulant dabigatran reduced osteoblast activity under optimal osteogenic conditions, including on titanium discs with a nanotopographic surface. Therefore, these observations suggest that anticoagulants may increase the revision rate by inducing osteolysis and impairing osseointegration of implants.

The present study had several limitations. First, it was a retrospective analysis. To minimize this limitation, we used prospectively collected patient data and blinded the senior author (J.W.L.) to the data collection and analysis. Second, the AOFAS Ankle-Hindfoot Scale score was used for functional evaluation. This score is not a validated scoring system. However, it is the most commonly used scoring system, so we included it for comparison with historical studies. Also, we used AOS scores in conjunction with AOFAS scores to help to overcome this potential limitation. Third, there was no control group of patients who underwent ankle arthrodesis or TAA using another prosthesis. However, it is difficult to have a control group for a long-term series such as this study. Lastly, the results of our analysis of risk factors for prosthesis failure require cautious interpretation. It is possible that some risk factors were not significant because of the small size of the prosthesis failure group. We also evaluated the risk factors for all revision surgery to compensate for this limitation. Further studies are required to clarify the exact pathophysiology of periprosthetic osteolysis after TAA, as this is a main reason for prosthesis failure and revision surgery.

In conclusion, TAA using the HINTEGRA prosthesis for the treatment of end-stage ankle arthritis produced satisfactory clinical results, which were maintained for ≥10 years. Although a number of revision and other procedures were performed, the overall functional outcomes and implant survivorship were promising. Our results also suggest that appropriate minor revision surgery may lengthen the survival period of the prosthesis.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org(http://links.lww.com/JBJS/H115). ■

Yeo Kwon Yoon, MD[1]
Kwang Hwan Park, MD, PhD[1]
Jae Han Park, MD[2]
Wonwoo Lee, MD[1]
Seung Hwan Han, MD, PhD[3]
Jin Woo Lee, MD, PhD[1]

[1]Department of Orthopaedic Surgery, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea

[2]Department of Orthopaedic Surgery, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, South Korea

[3]Department of Orthopaedic Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea

Email for corresponding author: ljwos@yuhs.ac

References

1. Glazebrook M, Daniels T, Younger A, Foote CJ, Penner M, Wing K, Lau J, Leighton R, Dunbar M. Comparison of health-related quality of life between patients with end-stage ankle and hip arthrosis. J Bone Joint Surg Am. 2008 Mar;90(3):499-505.
2. Kim HJ, Suh DH, Yang JH, Lee JW, Kim HJ, Ahn HS, Han SW, Choi GW. Total ankle arthroplasty versus ankle arthrodesis for the treatment of end-stage ankle arthritis: a meta-analysis of comparative studies. Int Orthop. 2017 Jan;41(1):101-9.
3. Stavrakis AI, SooHoo NF. Trends in complication rates following ankle arthrodesis and total ankle replacement. J Bone Joint Surg Am. 2016 Sep 7;98(17):1453-8.
4. Morash J, Walton DM, Glazebrook M. Ankle arthrodesis versus total ankle arthroplasty. Foot Ankle Clin. 2017 Jun;22(2):251-66.
5. Ahn J, Yoo MC, Seo J, Park M, Jeong BO. Comparison of total ankle arthroplasty and ankle arthrodesis in end-stage hemophilic arthropathy. Foot Ankle Int. 2020 Aug;41(8):937-44.
6. Shih CL, Chen SJ, Huang PJ. Clinical outcomes of total ankle arthroplasty versus ankle arthrodesis for the treatment of end-stage ankle arthritis in the last decade: a systematic review and meta-analysis. J Foot Ankle Surg. 2020 Sep-Oct;59(5):1032-9.
7. Hintermann B, Valderrabano V, Dereymaeker G, Dick W. The HINTEGRA ankle: rationale and short-term results of 122 consecutive ankles. Clin Orthop Relat Res. 2004 Jul;(424):57-68.
8. Barg A, Zwicky L, Knupp M, Henninger HB, Hintermann B. HINTEGRA total ankle replacement: survivorship analysis in 684 patients. J Bone Joint Surg Am. 2013 Jul 3;95(13):1175-83.
9. Choi WJ, Yoon HS, Lee JW. Techniques for managing varus and valgus malalignment during total ankle replacement. Clin Podiatr Med Surg. 2013 Jan;30(1):35-46.
10. Kim BS, Choi WJ, Kim YS, Lee JW. Total ankle replacement in moderate to severe varus deformity of the ankle. J Bone Joint Surg Br. 2009 Sep;91(9):1183-90.
11. Kim BS, Lee JW. Total ankle replacement for the varus unstable osteoarthritic ankle. Techniques in Foot and Ankle Surgery. 2010;9:157-64.
12. Domsic RT, Saltzman CL. Ankle Osteoarthritis Scale. Foot Ankle Int. 1998 Jul;19(7):466-71.
13. Kitaoka HB, Alexander IJ, Adelaar RS, Nunley JA, Myerson MS, Sanders M. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. Foot Ankle Int. 1994 Jul;15(7):349-53.

14. Henricson A, Carlsson A, Rydholm U. What is a revision of total ankle replacement? Foot Ankle Surg. 2011 Sep;17(3):99-102.

15. Doets HC, Brand R, Nelissen RG. Total ankle arthroplasty in inflammatory joint disease with use of two mobile-bearing designs. J Bone Joint Surg Am. 2006 Jun; 88(6):1272-84.

16. Yoon HS, Lee J, Choi WJ, Lee JW. Periprosthetic osteolysis after total ankle arthroplasty. Foot Ankle Int. 2014 Jan;35(1):14-21.

17. Yang HY, Wang SH, Lee KB. The HINTEGRA total ankle arthroplasty: functional outcomes and implant survivorship in 210 osteoarthritic ankles at a mean of 6.4 years. Bone Joint J. 2019 Jun;101-B(6):695-701.

18. Deleu PA, Devos Bevernage B, Gombault V, Maldague P, Leemrijse T. Intermediate-term results of mobile-bearing total ankle replacement. Foot Ankle Int. 2015 May;36(5):518-30.

19. Knecht SI, Estin M, Callaghan JJ, Zimmerman MB, Alliman KJ, Alvine FG, Saltzman CL. The Agility total ankle arthroplasty. Seven to sixteen-year follow-up. J Bone Joint Surg Am. 2004 Jun;86(6):1161-71.

20. Bianchi A, Martinelli N, Caboni E, Raggi G, Manfroni F, Sansone V. Long-term follow-up of Bologna-Oxford (BOX) total ankle arthroplasty. Int Orthop. 2021 May; 45(5):1223-31.

21. Lee GW, Wang SH, Lee KB. Comparison of intermediate to long-term outcomes of total ankle arthroplasty in ankles with preoperative varus, valgus, and neutral alignment. J Bone Joint Surg Am. 2018 May 16;100(10):835-42.

22. Daniels TR, Mayich DJ, Penner MJ. Intermediate to long-term outcomes of total ankle replacement with the Scandinavian Total Ankle Replacement (STAR). J Bone Joint Surg Am. 2015 Jun 3;97(11):895-903.

23. Nunley JA, Caputo AM, Easley ME, Cook C. Intermediate to long-term outcomes of the STAR total ankle replacement: the patient perspective. J Bone Joint Surg Am. 2012 Jan 4;94(1):43-8.

24. Clough T, Bodo K, Majeed H, Davenport J, Karski M. Survivorship and long-term outcome of a consecutive series of 200 Scandinavian Total Ankle Replacement (STAR) implants. Bone Joint J. 2019 Jan;101-B(1):47-54.

25. Valderrabano V, Pagenstert G, Horisberger M, Knupp M, Hintermann B. Sports and recreation activity of ankle arthritis patients before and after total ankle replacement. Am J Sports Med. 2006 Jun;34(6):993-9.

26. Dekker TJ, Hamid KS, Federer AE, Steele JR, Easley ME, Nunley JA, Adams SB Jr. The value of motion: patient-reported outcome measures are correlated with range of motion in total ankle replacement. Foot Ankle Spec. 2018 Oct;11(5):451-6.

27. Hendy BA, McDonald EL, Nicholson K, Rogero R, Shakked R, Pedowitz DI, Raikin SM. Improvement of outcomes during the first two years following total ankle arthroplasty. J Bone Joint Surg Am. 2018 Sep 5;100(17):1473-81.

28. Kim BS, Choi WJ, Kim J, Lee JW. Residual pain due to soft-tissue impingement after uncomplicated total ankle replacement. Bone Joint J. 2013 Mar;95-B(3):378-83.

29. Vulcano E, Myerson MS. The painful total ankle arthroplasty: a diagnostic and treatment algorithm. Bone Joint J. 2017 Jan;99-B(1):5-11.

30. Zafar MJ, Kallemose T, Benyahia M, Ebskov LB, Penny JO. 12-year survival analysis of 322 Hintegra total ankle arthroplasties from an independent center. Acta Orthop. 2020 Aug;91(4):444-9.

31. Zaidi R, Cro S, Gurusamy K, Siva N, Macgregor A, Henricson A, Goldberg A. The outcome of total ankle replacement: a systematic review and meta-analysis. Bone Joint J. 2013 Nov;95-B(11):1500-7.

32. McKenna BJ, Cook J, Cook EA, Crafton J, Knabel M, Swenson E, Miner S, Manning E, Basile P. Total ankle arthroplasty survivorship: a meta-analysis. J Foot Ankle Surg. 2020 Sep-Oct;59(5):1040-8.

33. Kerkhoff YR, Kosse NM, Metsaars WP, Louwerens JW. Long-term functional and radiographic outcome of a mobile bearing ankle prosthesis. Foot Ankle Int. 2016 Dec;37(12):1292-302.

34. Koivu H, Kohonen I, Mattila K, Loyttyniemi E, Tiusanen H. Long-term results of Scandinavian Total Ankle Replacement. Foot Ankle Int. 2017 Jul;38(7):723-31.

35. Kohonen Ia, Koivu H, Pudas T, Tiusanen H, Vahlberg T, Mattila K. Does computed tomography add information on radiographic analysis in detecting periprosthetic osteolysis after total ankle arthroplasty? Foot Ankle Int. 2013 Feb;34(2): 180-8.

36. Mehta N, Serino J, Hur ES, Smith S, Hamid KS, Lee S, Bohl DD. Pathogenesis, evaluation, and management of osteolysis following total ankle arthroplasty. Foot Ankle Int. 2021 Feb;42(2):230-42.

37. Cody EA, Bejarano-Pineda L, Lachman JR, Taylor MA, Gausden EB, DeOrio JK, Easley ME, Nunley JA 2nd. Risk factors for failure of total ankle arthroplasty with a minimum five years of follow-up. Foot Ankle Int. 2019 Mar;40(3): 249-58.

38. Lai WC, Arshi A, Ghorbanifarajzadeh A, Williams JR, Soohoo NF. Incidence and predictors of early complications following primary and revision total ankle arthroplasty. Foot Ankle Surg. 2019 Dec;25(6):785-9.

39. Gaugler M, Krähenbühl N, Barg A, Ruiz R, Horn-Lang T, Susdorf R, Dutilh G, Hintermann B. Effect of age on outcome and revision in total ankle arthroplasty. Bone Joint J. 2020 Jul;102-B(7):925-32.

40. Gigi R, Salai M, Dolkart O, Chechik O, Katzburg S, Stern N, Somjen D. The effects of direct factor Xa inhibitor (Rivaroxaban) on the human osteoblastic cell line SaOS2. Connect Tissue Res. 2012;53(6):446-50.

41. Apostu D, Lucaciu O, Lucaciu GD, Crisan B, Crisan L, Baciut M, Onisor F, Baciut G, Câmpian RS, Bran S. Systemic drugs that influence titanium implant osseointegration. Drug Metab Rev. 2017 Feb;49(1):92-104.

42. Sivagurunathan S, Pagel CN, Loh LH, Wijeyewickrema LC, Pike RN, Mackie EJ. Thrombin inhibits osteoclast differentiation through a non-proteolytic mechanism. J Mol Endocrinol. 2013 Apr 23;50(3):347-59.

43. Rocha AL, Bighetti-Trevisan RL, Duffles LF, de Arruda JAA, Taira TM, Assis BRD, Macari S, Diniz IMA, Beloti MM, Rosa AL, Fukada SY, Goulart GAC, Ribeiro DD, Abreu LG, Silva TA. Inhibitory effects of dabigatran etexilate, a direct thrombin inhibitor, on osteoclasts and osteoblasts. Thromb Res. 2020 Feb;186:45-53.