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Special Article

Medium-term results of the HINTEGRA total ankle arthroplasty

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Abstract

Objective: The aim of this study was to determine patient satisfaction, survivorship, and revision rate of the HINTEGRA total ankle arthroplasty (TAA). Our secondary objective was to assess hindfoot function.

Methods: All patients who underwent a HINTEGRA TAA between 2007 and 2014 were evaluated. We included a total of 69 patients (69 ankles), who were subjected to clinical and radiological examination and completed a visual analogue scale (VAS) for pain, the American Orthopaedic Foot and Ankle Society (AOFAS) ankle score, and the self-reported foot and ankle score (SEFAS). Hindfoot function was assessed using the AOFAS hindfoot score. Mean follow-up was 62 (57-101) months.

Results: The mean VAS score was 2 (0-3) and the SEFAS was 37 (26-48) at the most recent follow-up, while the AOFAS ankle score improved from 57 (52-62) to 87 (82-93). The AOFAS hindfoot score improved from 82 to 92 postoperatively. Eight patients had periprosthetic osteolysis and 5 underwent bone grafting of cysts. We detected polyethylene and hydroxyapatite particles in specimens obtained from the cysts. Eight patients had their procedures converted to an ankle arthrodesis.

Conclusion: In select patients, TAA improved quality of life. Our medium-term follow-up of the HINTEGRA TAA observed a survivorship of 89% at 5 years with an improvement in the AOFAS score and a mean SEFAS score of 37. We recommend that large periprosthetic cysts, which may be caused by the hydroxyapatite coating and polyethylene particles, be bone grafted prophylactically. We found hindfoot function to be preserved.

Level of Evidence IV; Therapeutic Studies; Case Series.

Keywords: Arthroplasty; Osteolysis; Arthroplasty, Replacement, Ankle.

Introduction

The occurrence of primary osteoarthritis (OA) is not as common as post-traumatic OA of the ankle. The Canadian Orthopaedic Foot and Ankle Society classification for ankle arthritis includes deformities and the involvement of the neighboring joints in conjunction with ankle arthritis. This classification is currently widely used and has substituted previous classifications[1,2]. Secondary OA of the hip and knee joints accounts for only 9.8% and 1.6% of OA cases, respectively, whereas in the ankle it is reported to be as high as 65%-80%[3-6]. This progressive destructive joint disease leads to severe pain, decreased quality of life, and limits the performance of activities of daily living. The impact and severity of ankle OA is reported to be equivalent to those of end-stage renal disease or congestive cardiac failure[7-10].

The management of end-stage ankle arthritis includes fusion and total ankle arthroplasty (TAA). Following the abysmal failures of first-generation TAA designs, there has been a resurgence of TAA in the orthopaedic foot and ankle community using third-generation implants[1]. The HINTEGRA TAA, in particular, was designed to allow for less bone resection and a better surgical technique with a potentially longer survivorship. As is commonly seen in the literature, majority of the published data regarding TAA comes from the designing surgeons, the Hintegra TAA is no different[1,2,4-6,11]. These publications often report better survivorship than that reported by general surgeons. Medium-term results of the HINTEGRA TAA, as reported by the designers, included an 84% patient satisfaction[9]. Outcomes from non-designer surgeons also needs to be reported. It is necessary to report the clinical outcome of TAA as a quality measure and not only by revision rates[11].

Study performed at the University of the Witwatersrand, Johannesburg, Gauteng, South Africa.

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The aim of this retrospective study was to determine patient satisfaction, survivorship, and revision rate of the HINTEGRA TAA in the medium-term. Our secondary objective was to assess hindfoot function following TAA using the HINTEGRA prosthesis.

Methods

This study was approved by the Human Research Ethics Committee under the Clearance Certificate number: M170862.

All TAA procedures performed by a sole surgeon (NPS) using the HINTEGRA TAA prosthesis between 2007 and 2014 were identified. This research project was approved by the institution's ethics and research committee. Exclusion criteria included incomplete patient records and patients who were unavailable for follow up or who received protheses other than the HINTEGRA. A total of 93 TAA procedures using the HINTEGRA prothesis were performed during this period. Eight patients had passed away with a mean implant retention of 76 (72-80) months and 16 patients were untraceable. Sixty-nine patients (69 ankles) - 28 women (40.58%) and 41 men (59.42%) were included in the study (Figure 1).

Patient age ranged from 42 to 77 years, with a mean of 65 years. Patient demographics and indications for TAA are outlined in table 1. All patients were followed up on an annual basis after the first year. The mean follow-up time was 62 (57-101) months.

All patients underwent clinical and radiological assessments. Radiological assessment consisted of standard weight-bearing foot and ankle views, and radiographic alignment was measured on all X-ray images (Figure 2). The American Orthopaedic Foot and Ankle Society (AOFAS) ankle score, visual analogue scale (VAS), and self-reported foot and ankle score (SEFAS) were recorded for all patients. For evaluating hindfoot function, preoperative and postoperative AOFAS hindfoot scores were compared. Clinical examinations were performed, and data were collected by the author (MK). Preoperative data was obtained from medical records.

All data were assembled on a Microsoft Excel spreadsheet prior to analysis using STATA version 14. For continuous demographic variables, the Shapiro-Wilk test was used to check for the normality of the data and for deciding on whether to report them as means and standard deviations (SDs) or medians and interquartile ranges (IQR). For categorical variables, frequency tables were computed to determine the proportions for each demographic/clinical category. Differences between preoperative and postoperative AOFAS ankle scores were calculated and checked for normality. They were found to be normally distributed - hence a paired t-test was used to analyze the differences between preoperative and postoperative scores. AOFAS hindfoot scores were compared pre- and postoperatively, and the differences were found to be normally distributed; a paired t-test was also used analyze these results.

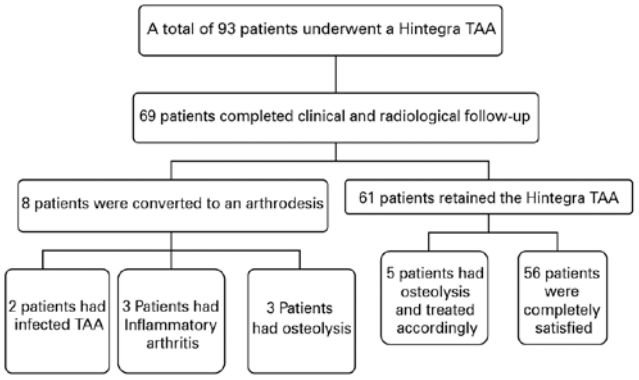

Figure 1. Flowchart of study outcomes.

Table 1. Patient demographics and indications for TAA

Characteristics	Number (N=69)
Sex	
Female	28
Male	41
Side	
Left	34
Right	35
Diagnosis	
Post-traumatic OA	60
Primary OA	6
Inflammatory arthritis	3

TAA: total ankle arthroplasty; OA: osteoarthritis.

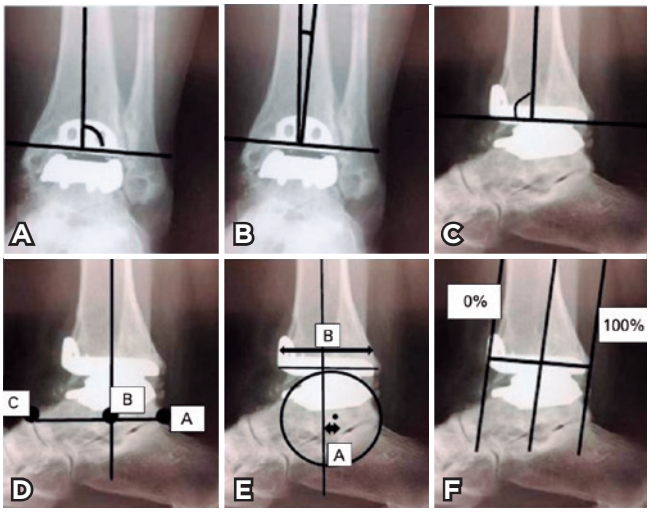

Figure 2. Methods of measurement of postoperative implant sagittal and coronal alignment: A. anatomic lateral distal tibial angle; B. tibiotalar angle; C. anatomic anterior distal tibial angle; D. tibial axis–talus ratio (tibiotalar ratio: AB/AC); E. anteroposterior offset ratio measurement (A/B); F. contact point ratio.

Results

Post-traumatic OA of the ankle joint was found to be the most common indication for TAA in our series. Three patients had inflammatory arthritis, of which 1 had systemic lupus erythematosus (SLE) and the other 2 had rheumatoid arthritis. These patients were on appropriate medical treatment, including biologic agents, in the perioperative period; a biologics-free window of three dosing cycles was strictly adhered to before surgery.

The mean AOFAS ankle score was 57 (range: 52.18-61.99) preoperatively, and 87 (range: 82.25-92.31) postoperatively; there was significant improvement after surgery (p-value <0.0001). The mean SEFAS score, representing patient satisfaction, was 37 (range: 26-48). A SEFAS score of 0 indicates severe disability and a score of 48 indicates normal function. According to these scores, 88% of the patients reported excellent or good outcomes (results are summarized in table 2). The median visual analogue pain score was 2 (0-4). The AOFAS hindfoot score improved significantly from 82 (range: 80-84) preoperatively to 92 (range: 90-94) post-surgery (p-value <0.0001). Patients had a mean ankle range of motion (ROM) of 37° before surgery and 32º after the procedure; ankle ROM thus did not improve after TAA in our series. Ankle instability was clinically checked through anterior drawer and varus stress tests and was not observed in any of the patients.

The radiographic alignment of the implant is summarized in Table 3. Two cases presented talar component subsidence, but with no clinical sequelae. At radiographic evaluation, 1 patient showed midfoot arthritis, 1 presented posterior subluxation of the ankle joint (clinically stable), and 1 had a worn polyethylene (PE) liner. These patients did not require additional surgery as they were asymptomatic and fully functional.

Table 2. SEFAS scores

SEFAS score	Outcome	Number of patients (N=69)
>40	Excellent	56
30-39	Good	5
20-29	Average	8
>20	Poor	**0**

SEFAS: self- reported foot and ankle score.

Table 3. Radiographic measurements of preoperative and postoperative ankle alignment

X-ray measurement	Preoperative	Postoperative	Normal value[8]
Anatomic lateral distal tibial angle	86-94° (mean: 90°)	85-93° (mean: 94°)	85-95°
Tibiotalar angle	-10-10 ° (mean: 0°)	0-6° (mean: 3°)	-5-+5°
Anatomic anterior distal tibial angle	78-92° (mean: 90°)	85-93° (mean: 89°)	80-90°
Tibial axis–talus ratio	28-46 (mean: 42)	34-50 (mean: 42)	27-42%
Anteroposterior offset ratio	-2-+3 (mean: 1)	0.1-0.2 (mean: 0.15)	0
Contact point ratio		35-50 (mean: 42.5)	40-45%

Eight patients were found to have developed large cysts (10mm^2 or larger) around their implants on postoperative follow-up X-ray imaging. These cysts were classified according to the Gruen zones (Figure 3). Three patients refused any further interventions, as they were asymptomatic. The other 5 patients underwent bone grafting of the cysts using a combination of allograft bone chips and demineralized bone matrix. A CT Scan was obtained for all patients prior to surgery, for planning purposes. Specimens from all five cases were sent for histology requesting Hematoxylin and Eosin (H&E) staining, Von Kossa staining, polarized light microscopy and Oil Red O (ORO) staining.

At H&E staining, serial sections showed synovium with aggregated clusters of pigmented crystalline-like material associated with a foreign body granulomatous response (Figure 4A). These clusters were found to be positive in Von Kossa staining, indicating the presence of of hydroxyapatite (Figure 4B). We identified PE particles in 3 out of the 5 specimens using ORO and polarized microscopy (Figure 4C and D).

Three patients had superficial wound infections. These occurred within the first 2 weeks, were treated topically and with oral antibiotics, and subsequently healed. A total of 8 patients had failure of the TAA and were converted to a fusion. Two cases developed deep infections within 1 year of the index surgery. These were referred to the sepsis unit for management and, once cleared of the infection (6-8 weeks), were converted to an allograft bone block arthrodesis by the primary surgeon. All 3 patients with inflammatory arthritis had their TAA procedures converted to ankle arthrodesis due to aseptic loosening within 2-5 years after index TAA surgery. Other 3 patients developed aseptic loosening with bone loss and required conversion to a fusion. The complications encountered in our case series were classified according to Glazebrook et al.[2] were summarized in table 4.

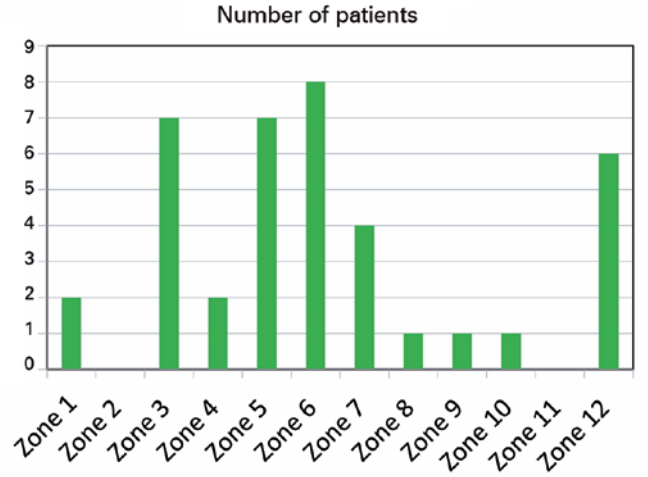

Figure 3. Distribution of cysts according to Gruen zones in the 8 patients who presented with osteolysis.

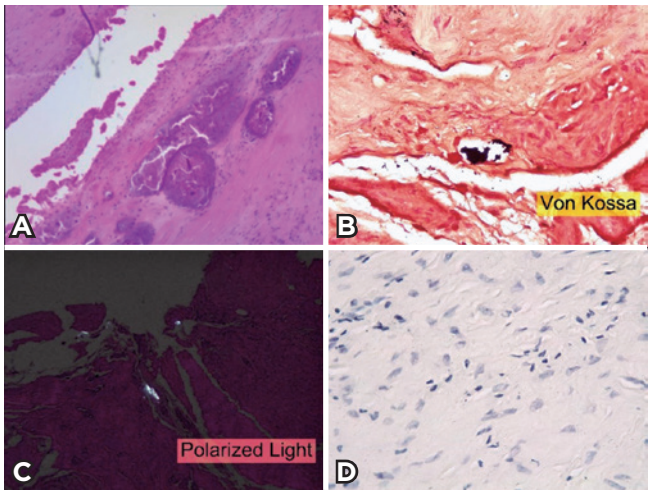

Figure 4. A. Hematoxylin and eosin (H&E) staining of the periprosthetic cysts reveals clusters of pigmented crystalline-like material associated with a foreign body granulomatous response. B. Von Kossa staining of periprosthetic osteolytic cysts showed multiple calcified layers. C. Birefringent particles under polarized microscopy of the periprosthetic osteolytic cysts showed polyethylene particles. D. Oil red O (ORO) staining of specimen taken from a patient with periprosthetic osteolysis around the HINTEGRA prosthesis.

Table 4. Complications according to Glazebrook's classification[2]

Complications	Number
High-grade complications	
Deep infection	2
Aseptic loosening	6
Implant failure	8
Medium-grade complications	
Technical error	0
Subsidence	2
Postoperative fracture	0
Low-grade complications	
Intraoperative fracture	0
Wound healing problems	3

Survivorship of the HINTEGRA implant at 62 months was 89% and the reoperation rate was 7%. No revisions of the implant components have been performed at this stage. Out of all TAAs, 11.4% failed and needed to be converted to ankle fusion. Fifty-six (90.80%) patients would strongly recommend a TAA to another patient. Five patients (8.20%) would not recommend this surgery, mainly due to a long perceived recovery.

Discussion

Fuchs and colleagues, in their 20-year follow-up study on ankle arthrodesis, found a significant negative impact not only on activities of daily living but also on patients' emotional aspects[7]. Total ankle arthroplasty is expected to improve quality of life, decrease pain, and improve gait[11]. The first TAA was performed by Lord and Marotte in 1970 using an inverted hip prosthesis, with disappointing results[7,9,11-13]. Dedicated first-generation TAA implants had constrained designs; these cemented prosthesis with constrained bearings did not have great medium- to long-term outcomes, with a high failure rate due to loosening[11,13-15]. Since then, designers have developed new implants, with different geometries and new technologies such as cementless interfaces and mobile bearings. Semi-constrained and non-constrained implants allow for additional axial rotation[14]. The Agility Total Ankle system, Salto Talaris, and Inbone are two-component prostheses as they have a fixed bearing surface. The Scandinavian Total Ankle Replacement (STAR) and HINTEGRA are three-component prostheses with a mobile bearing. It is important to note that medium-term follow-up of fixed-bearing and mobile-bearing implants revealed no differences in functional tests or outcomes[5,6,16-19]. Patient satisfaction increased from 10% and 65% (in patients with first- and second-generation implants, respectively) to almost 90% with third-generation implants such as the HINTEGRA TAA[3,13,18,20-24].

The ideal candidate for TAA is a mobile, middle-aged, or older patient with no significant comorbidities, good bone stock, and a stable and well-aligned arthritic ankle[14-17,25-29]. Total hip arthroplasty has a good outcome in patients younger than 30 years old, and total knee arthroplasty indications have been extended for patients younger than 55 years old. Kofoed and colleagues believe that TAA in the younger patient presents similar longevity and clinical outcomes as that performed in older patients. TAA has a good reported survivorship and longevity in patients as young as 42 years old[30-32]. The authors feel that the improved function, sparing of the hindfoot joints, and possibility of converting the TAA to an arthrodesis later, if required, render age a relative contraindication for TAA. This has also been reported by Latham and colleagues[23].

Minimal bone resection is a primary requirement for a good ankle prosthesis together with proper soft tissue balancing and alignment for a successful outcome[5]. The HINTEGRA total ankle replacement has one of the least constrained three-component prosthesis designs. Biomechanically, this implant provides axial rotation, as well as flexion and extension. It has been shown to be stable with eversion and inversion. The prosthesis involves minimal bone resection with stable fixation, which does not require cementing or intramedullary fixation, thus making the surgery technically easier[1,9,12,17,33-36].

Patients with arthritis in the neighboring joints (subtalar or midtarsal), in the knee, hip, or contralateral ankle will benefit more from TAA than from an arthrodesis procedure[1,4,22]. The HINTEGRA total ankle replacement is a good alternative to ankle arthrodesis. Preserving motion in the ankle joint with

a TAA decreases the strain on neighboring joints. Although the published literature suggests that the ROM of the ankle joint can increase after TAA, our study found no significant postoperative increase in ankle ROM. The first audit of the HINTEGRA TAA by the designers also reported limited dorsiflexion[1,5,12-13]. This procedure can also preserve the biomechanics of the hindfoot and generally help patients improve their function, decrease pain, and discomfort, overall improving quality of life[7,11,37-38]. In our study, the AOFAS hindfoot score improved from 82 to 92 after TAA, thus confirming that hindfoot function was preserved and even suggesting that it improved.

Early failure of TAA is commonly due to infection or surgical errors, whereas late failure is due to aseptic loosening[13,27,28]. In a study done by Braito et al., 15% of TAA failures were found to be due to aseptic loosening; researchers concluded that this was the most common cause of TAA failure[37]. Hintermann and colleagues described radiographic criteria for loosening of the implant: The tibial component should be considered loose if either its position has changed by more than 2° relative to the long axis of the tibia, or a progressive radiolucency of more than 2mm is detected around the implant on anteroposterior or lateral views. The criteria for a loose talar component are: subsidence greater than 5 mm or a change in position of more than 5° relative to the hindfoot axis[3,13,21]. Other studies have suggested possible implant loosening when components moved more than 5° or 5 mm in serial X-ray imaging[27-28,33]. In our series, we had 6 cases of aseptic loosening that required conversion to fusion. Interestingly, the 3 patients in our cohort who had inflammatory arthritis all developed aseptic loosening. This is in contrast with Doets et al., who reported that the results of TAA in patients with rheumatoid arthritis were similar to those in patients with osteoarthritis[20]. We had 2 cases with talar component subsidence; both were asymptomatic patients with normal ankle function.

Periprosthetic cysts have been correlated with TAA failure, especially in mobile-bearing prostheses. Although the exact pathophysiology of this cyst formation is not fully understood, several hypotheses have been described[25]. From a mechanical point of view, osteolysis starts with the mechanical wear of the articulating surfaces and progresses with a cell-mediated immunological response to the wear particles. Particle disease, which is due to a reaction to the PE component, has been reported. According to this theory, cytokines are released by activated macrophages (histiocytes) after phagocytosing PE particles. The cytokines activate osteoclasts and inhibit osteoblast activity, leading to periprosthetic bone lysis[3,21,25,35-36]. The biological response by the host depends on particle size and concentration[3,21]. A gradual increase in fluid pressure occurs due to the inflammatory process, which leads to more bone loss[3,36]. Singh et al. used the term "ballooning osteolysis" to describe large periarticular cystic lesions found during revision TAA. They believe that the osteolysis mechanism in TAA is different than that in other joint arthroplasty procedures due to the difference in biomechanics[36].

Gruen and colleagues described radiographic zones for easier assessment and research of osteolysis after TAA[3,21,35] (Figure 5). In our study, zone 6 followed by zones 3 and 5, were the most commonly affected by osteolysis. Osteolytic cysts around the implant are more difficult to diagnose on plain X-ray images as they can be obscured by the tibial and talar components. Hanna and colleagues observed that CT scans with metal artefact suppression were more sensitive and accurate than plain radiography and should be used for assessing osteolysis in all cases[15]. Jensen and colleagues advocated using 3D multiplanar reconstructed images instead of CT scans to address the issue of scattering related to the CT scan[26]. We identified 8 patients with large periprosthetic cysts on X-ray imaging, of which 5 had had a CT scan.

Singh and colleagues reported on the histomorphometric, immunohistochemical, and elemental analyses of tissues from failed TAA procedures due to osteolysis. Von Kossa staining was used instead of H&E staining. They concluded that the implant's hydroxyapatite coating contributed to cyst formation[36]. All five specimens collected in our study yielded positive Von Kossa staining results, supporting the theory that hydroxyapatite plays a causative role in periprosthetic osteolysis and cyst formation.

Another similar histologic study on osteolytic cysts and periarticular tissue when using the Ankle Evolutive System (AES) prosthesis showed that Al_2O_3 particles released from sand blasting may cause cracks in the titanium/titanium oxide coating, thereby producing stress concentrations that lead to osteolysis[4,17,35]. Dalat et al., in their study on osteolysis around the AES, found metal debris and PE particles within the obtained samples[16].

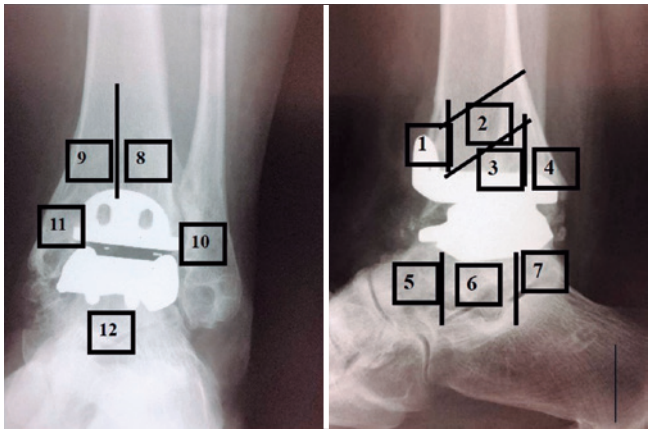

Figure 5. Osteolytic zones in the tibia and talus, according to Gruen and colleagues. Zones 2 and 5 were recommended for screw insertion by the initial HINTEGRA TAA surgical technique. Due to a high rate of osteolysis around these screws, these optional fixation screws were abandoned.

Histiocytes and giant cells are the most common cells observed in these cysts. Histologic studies have shown PE and metal particles in the samples[3,36]. Schmalzried et al. observed that ORO staining had a similar sensitivity to polarized microscopy but was less specific for identifying PE particles; they recommended that the ORO staining should not be used as an isolated method for identifying PE particles. However, Schipper et al. reported that this staining technique was very specific (96.4%) and sensitive (100%)[8,27-28]. Van Wijngaarden et al. also detected PE particles in all their samples using the ORO staining method[10]. Our experience regarding the ORO staining method, used in isolation, differs from that of Schipper et al., as we observed PE particles in only 3 specimens. We found the combination of ORO and polarized microscopy to be more sensitive and specific for identifying PE particles.

Prosthetic design and surgical technique have been shown to influence the development of osteolysis[13,17,22]. We assessed implant alignment using radiographs of the 8 patients who developed osteolysis and found no obvious malalignment that could have contributed to cyst formation. Various studies confirmed that most of the periprosthetic osteolytic cysts related to the HINTEGRA TAA were asymptomatic. However, these cysts should still be identified and treated accordingly. Patient age, weight, and activity level have been reported as risk factors for progression.

Treatment of osteolytic cysts after TAA is challenging. Options can be broadly divided into monitoring, bone grafting, revision, or conversion of the TAA to arthrodesis. If the defect is contained, then bone grafting is the preferred option. A segmental defect, on the other hand, might require revision of the implant. Implants needed for revising a TAA are technically challenging[21,33-34]. Hintermann et al. published a revision protocol for the HINTEGRA TAA in 2013[12]. Gross and colleagues reported that grafting of periprosthetic bone cysts without revision of the prosthesis was effective and increased implant survivorship[33]. In our study, we bone grafted 5 of the 8 periprosthetic cysts with good early results.

In our series, the AOFAS ankle score significantly improved from 57 preoperatively to 84 postoperatively. This is comparable to several other designer and non-designer studies[4,24]. Our results are similar to those of Jung et al., who reported 90.5% of satisfaction in their medium-term follow-up[3,14]. Our postoperative AOFAS ankle scores and survival rates were similar to those of previous studies on the HINTEGRA TAA (Table 5).

Survivorship of a TAA is defined as metallic component failure requiring prosthesis removal and conversion to an arthrodesis, while revision of a TAA is defined as the exchange of one or more components (including the plastic component) without any known trauma[38]. Good short- to medium-term results were reported by European surgeons using the STAR TAA: Wood and Deakin reported a survival rate of 80.3% and Karantana et al. reported a survival rate of 84% with a minimum follow-up of 10 years[39]. A non-designer short-term follow-up study in South Africa showed very satisfactory results for the STAR prosthesis, with survival rates of 95.6%[40]. The survivorship of the HINTEGRA prosthesis in our study was 89% at 62 months, with a 95% confidence interval (Kaplan-Meier curve, Figure 6). Overall survivorship reported in designer studies was 78%-94% and 77%-84% after 5 and 10 years, respectively[1,41]. Survival rates for modern TAA range from 69% to 79% after 10 years; in comparison, total hip and knee arthroplasties present a 95% survivorship[19,21].

Table 5. Comparison of survival rates and postoperative AOFAS ankle scores between the literature and the current study

Study	Year of publication	Type of study	Survival rate	Postoperative AOFAS score	Sample size
Hintermann et al.[26]	2004	Short-term	94%	85	122
Nery et al.[48]	2010	Short-term	94%	76	10
Bai et al.[3]	2010	Short-term	97%	86	65
Choi et al.[35]	2013	Short-term	87.5%	82	21
Barg et al.[4]	2013	Medium-term	94%		684
Hintermann et al.[27]	2013	Medium-term	83%		117
Current study	2020	Medium-term	89%	92	69

AOFAS: American Orthopaedic Foot and Ankle Society.

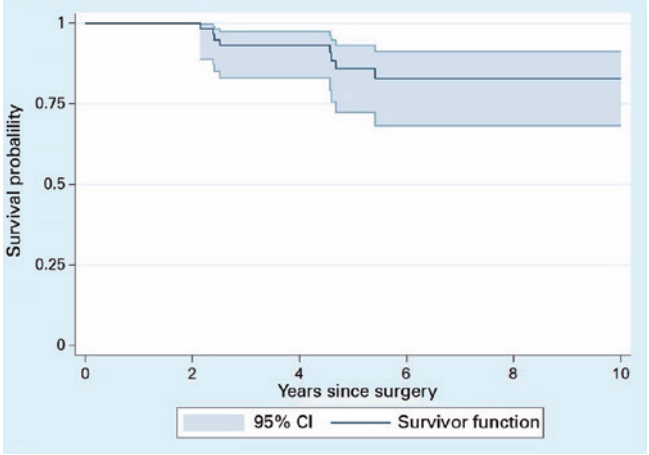

Figure 6. Kaplan-Meier curve showing 89% survivorship in our case series, with a 95% confidence interval (CI).

Conclusion

In select patients, TAA improved quality of life and had good longevity. Our medium-term follow-up of the HINTEGRA TAA showed that the prosthesis had a survivorship of 89% at 5 years, with significant improvement in the AOFAS ankle score (57 to 84) and 88% of patients reporting excellent or good outcomes. We recommend that large periprosthetic cysts (>10 mm^2) be bone grafted prophylactically when identified. Although the pathophysiology of aseptic loosening is still not fully understood, we believe that hydroxyapatite coating and PE wear particles could be causative factors. As a secondary aim of our study, we found hindfoot function to be preserved, with significant improvement in the follow-up AOFAS hindfoot scores.

Authors' Contributions: Each author contributed individually and significantly to the development of this article: KM *(https://orcid.org/0000-0003-3167-7797) collected data; interpreted the results; wrote the paper; participated in the reviewing process; approved the final version; NPS *(https://orcid.org/0000-0002-5566-7588) conceived and planned the activities that led to the study; participated in the reviewing process; approved the final version; PNFF *(https://orcid.org/0000-0003-4639-0326) conceived and planned the activities that led to the study; participated in the reviewing process; approved the final version. *ORCID (Open Researcher and Contributor ID).

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