Does Gender Influence the Outcomes of Total Ankle Arthroplasty in Patients with Ankle Osteoarthritis?

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Abstract

Background Total ankle arthroplasty has progressed as a treatment option for patients with ankle osteoarthritis. However, no studies have been conducted to evaluate the effect of gender on the outcome. The purpose of the present study was to evaluate outcomes, survivorship, and complications rates of total ankle arthroplasty, according to gender differences.

Methods This study included 187 patients (195 ankles) that underwent mobile-bearing HINTEGRA prosthesis at a mean follow-up of 7.5 years (range, 4 to 14). The two groups consisted of a men's group (106 patients, 109 ankles) and a women's group (81 patients, 86 ankles). Average age was 64.4 years (range, 45 to 83).

Results Clinical scores on the Ankle Osteoarthritis Scale for pain and disability, and American Orthopaedic Foot and Ankle Society ankle-hindfoot score improved and were not significantly different between the two groups at the final follow-up. There were no significant differences in complication rates and implant survivorship between the two groups. The overall survival rate was 96.4% in men and 93.4% in women at a mean follow-up of 7.5 years (p=0.621).

Conclusions Clinical outcomes, complication rates, and survivorship of total ankle arthroplasty were comparable between men and women. These results suggest that gender did not seem affect outcomes of total ankle arthroplasty in patients with ankle osteoarthritis.

Background

Ankle osteoarthritis is a slowly progressive destructive disease inducing pain, dysfunction, impaired mobility, and decreased quality of life.[1] Compared to ankle arthrodesis, total ankle arthroplasty (TAA) can preserve gait motion by restoring closer to normal joint motion and improve patient satisfaction by reducing pain while minimizing subtalar joint arthritis.[2–7] Several recent studies reported satisfactory outcomes of TAA, these promising outcomes have led TAA as a primary treatment option for ankle osteoarthritis.[8–17]

Various predisposing factors including age, gender, and preoperative deformity can affect the outcome of TAA.[9, 11, 17–21] In related to gender difference, several studies demonstrated divergent clinical outcomes following total hip or total knee arthroplasty. In total hip arthroplasty,
some studies reported no difference in all postoperative outcome measures between men and women.[22] On the other hand, another study reported that gender-related analysis resulted in significantly higher scores for men compared to women.[23] Recent meta-analysis demonstrated that men showed a higher risk of revision after primary total hip arthroplasty due to any cause, infection, or aseptic loosening, when compared to women.[24] In terms of total knee arthroplasty, several studies reported that functional outcomes were different between men and women.[25-27] On the contrary, another study suggested that gender does not seem to affect clinical outcome.[28] However, no study has been conducted examining the outcomes of gender-based differences in TAA. We hypothesize that clinical and radiographic outcomes for TAA would be comparable between men and women patients. Thus, the purpose of the present study was to compare intermediate-term clinical and radiographic outcomes, survivorship, and complications rates of TAA in patients with end-stage ankle osteoarthritis according to gender differences.

Materials And Methods
This study was approved by the Institutional Review Board of our hospital. Informed consent was obtained from all patients. Between January 2005 and December 2015, a total of 243 consecutive primary TAA were performed in 231 patients using cementless three-component HINTEGRA prosthesis (Newdeal, Lyon, France/Integra Lifesciences, Plainsboro, NJ, USA). Inclusion criteria were symptomatic end-stage ankle osteoarthritis with a minimum follow-up of 48 months after TAA, and fulfillment of general total ankle arthroplasty indications including good bone stock and normal neurovascular status. Patients were excluded from the trial if they had any of the following: secondary osteoarthritis due to osteonecrosis of the talus or pigmented villonodular synovitis; arthritis caused by systemic disease, such as rheumatoid arthritis and hemophilia; and previous history of infectious arthritis or ankle arthrodesis.

Finally, we enrolled 187 patients (195 ankles) who underwent primary TAA. We divided the patients into two groups according to gender: (1) men’s group (106 patients, 109 ankles) and (2) women’s group (81 patients, 86 ankles). Patients in each group showed similar characteristics in mean age, preoperative diagnosis, and follow-up duration (Table 1).
Table 1
Comparison of Patient Demographics between Men and Women

|                        | Men (N = 109 ankles) | Women (N = 86 ankles) | P value* |
|------------------------|----------------------|-----------------------|----------|
| Age (year)†            | 65.4 ± 7.3 (45 to 82) | 63.2 ± 7.2 (47 to 83) | 0.114    |
| BMI (kg/m²)†           | 25.3 ± 2.3 (20.5 to 31.8) | 25.6 ± 2.7 (19.1 to 32.0) | 0.111    |
| Diagnosis‡             |                      |                       | 0.277    |
| Primary osteoarthritis | 40 (36.7%)           | 31 (36.0%)            |          |
| Recurrent ankle sprain | 35 (32.1%)           | 20 (23.3%)            |          |
| Post-fracture          | 34 (31.2%)           | 35 (40.7%)            |          |
| Follow-up (months)†    | 90.3 ± 32.6 (48 to 170) | 89.6 ± 32.9 (50 to 174) | 0.887    |

BMI = body mass index.

*The independent t test was used to analyze age differences in age, BMI, and follow-up duration. The chi-square test was used to analyze differences in preoperative diagnoses. A p-value of < 0.05 was considered significant.
†The values are given as the mean ± standard deviation, with the range in parentheses.
‡The values are given as the number of ankles, with the percentage in parentheses.

Surgical Technique and Postoperative Management

Patients underwent TAA with HINTEGRA prosthesis by a single surgeon, with use of a longitudinal anterior approach between the anterior tibial tendon and the extensor hallucis longus, with the patient in the supine position. After removal of anterior capsular synovial tissue and osteophytes, the tibial cut was performed perpendicular to the mechanical axis of the tibia. The talus bone cut was made parallel to the tibial cut, then the medial, lateral and posterior talar cuts were made. After selected components had been inserted, the alignment, stability, joint motion, and implant position were checked by an image intensifier. Hindfoot alignment and ligamentous stability were rechecked. Concomitant procedures were done to obtain neutral alignment, stability, and ligamentous balance, if necessary.

Postoperatively, for the first postoperative two weeks, a short leg splint was worn and patients maintained non-weight-bearing with neutral ankle positions. For the next four weeks, patients were allowed to begin range of motion (ROM) exercises. At six weeks after surgery, progressive weight-bearing ambulation was initiated with ankle-foot orthosis. The rehabilitation protocol differed slightly if additional procedures were performed at the index surgery.

Clinical Evaluation

Ankle Osteoarthritis Scale (AOS) pain and disability,[29] American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot scoring system,[30] Short Form (SF)-36 Physical Component Summary score (PCS),[31] and Visual Analogue Scale (VAS) for pain were administered to the patients for assessment of clinical outcomes. ROM of ankle joint, including degree of dorsiflexion and plantar flexion was
measured using a goniometer along the lateral border of the leg and foot. The main outcomes were assessed based on the AOS, because it was reliable, validated, and an ankle joint-specific measurement. The AOFAS scoring system, a combination of subjective and objective data, was used as secondary assessment tool. SF-36 scores and VAS pain were utilized as comparative measures. This study noted postoperative complications, and it were divided into major and minor. Major complications included deep infection, periprosthetic osteolysis and its associated complication. Minor complications included wound problems and heterotopic ossification.[32, 33] We defined failure when either the tibial or talar metallic component was replaced.[19]

**Radiographic Evaluation**
Radiographic examination included anteroposterior and lateral radiographs of the ankle on full weight-bearing, taken preoperatively and postoperatively. Follow-up radiographs were taken at 1, 3, 6, and 12 months postoperatively, and annually thereafter. The coronal plane alignment was determined from the angle formed between the anatomical axis of the tibia and a line perpendicular to the talus or talar component. For the radiographic analysis, measurements were made using a PACS (picture archiving and communication system: Maroview 5.4; INFINITT Healthcare). To minimize measurement errors, by two independent observers measured radiographic values twice and the mean of the remaining values except the maximum and the minimum was reported.

**Statistical Analysis**
Descriptive statistics were calculated by use of standard formulas. A Kolmogorov-Smirnov test was used to verify that data were normally distributed. For normally distributed variables, the independent t-test was used to determine the significance of intergroup differences. The Mann-Whitney U test was used to analyze differences when there was a lack of normality. For the categorical variables, Chi-square tests or Fisher’s exact test was used to analyze differences. Data were analyzed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Statistical significance was accepted for p values < 0.05, and all components of the statistical analysis were reviewed by a statistician.

**Results**
**Clinical Outcomes**
The clinical outcome details are provided in Table 2 (Fig. 1). The mean preoperative AOS pain scores
were 57.6 points in men and 58.6 points in women, and these were improved to 17.6 and 22.4 points, respectively, at final follow-up. The mean AOS disability scores were 67.3 points in men and 65.2 points in women, and these were improved to 28.3 and 32.1 points, respectively, at final follow-up. The preoperative AOFAS scores were improved to 88.3 points in men and 83.9 points in women at final follow-up. The SF-36 PCS was improved by 23.2 points in men and 8.8 points in women. The VAS pain score was also improved to 1.7 points in men and 2.0 points in women at final follow-up. There was no significant difference in clinical outcomes and ROM between the two groups at the final follow-up, except for SF-36 PCS (p < 0.05).

### Table 2

| Clinical Outcomes of the Men and Women Groups | Men (N = 109 ankles) | Women (N = 86 ankles) | P value* |
|-----------------------------------------------|---------------------|-----------------------|----------|
| AOS Pain†                                     |                     |                       |          |
| Preoperative                                  | 57.6 ± 14.95        | 58.6 ± 17.36          | 0.907    |
| Final follow-up                               | 17.6 ± 19.29        | 22.4 ± 21.37          | 0.178    |
| AOS Disability†                                |                     |                       |          |
| Preoperative                                  | 67.3 ± 11.29        | 65.2 ± 14.63          | 0.669    |
| Final follow-up                               | 28.3 ± 20.88        | 32.1 ± 23.05          | 0.366    |
| AOFAS ankle-hindfoot score†                    |                     |                       |          |
| Preoperative                                  | 51.0 ± 13.92        | 52.3 ± 12.54          | 0.573    |
| Final follow-up                               | 88.3 ± 11.99        | 83.9 ± 15.16          | 0.060    |
| SF-36 PCS score†                               |                     |                       |          |
| Preoperative                                  | 41.9 ± 15.92        | 46.7 ± 16.45          | 0.149    |
| Final follow-up                               | 65.2 ± 22.32        | 55.4 ± 25.05          | 0.027    |
| VAS pain†                                     |                     |                       |          |
| Preoperative                                  | 6.8 ± 1.83          | 7.0 ± 1.61            | 0.534    |
| Final follow-up                               | 1.7 ± 2.28          | 2.0 ± 2.25            | 0.272    |
| ROM, Dorsiflexion (deg)†                       |                     |                       |          |
| Preoperative                                  | 9.8 ± 6.20          | 9.6 ± 5.44            | 0.877    |
| Final follow-up                               | 10.5 ± 6.24         | 11.3 ± 5.12           | 0.381    |
| ROM, Plantar flexion (deg)†                   |                     |                       |          |
| Preoperative                                  | 21.4 ± 10.09        | 23.9 ± 9.94           | 0.138    |
| Final follow-up                               | 22.8 ± 11.28        | 25.6 ± 9.84           | 0.170    |

AOS = Ankle Osteoarthritis Scale; AOFAS = American Orthopaedic Foot & Ankle Society; SF-36 PCS = Short Form-36 Physical Component Summary; VAS = Visual Analogue Scale; ROM = range of motion

*The independent t test was used to analyze age differences in all variables except range of motion. The Mann-Whitney U test was used to analyze differences in range of motion. A p-value of < 0.05 was considered significant.

†The values are given as the mean ± standard deviation.

### Radiographic Outcomes

The radiographic outcome details are provided in Table 3. The mean tibiotalar angle of each group was 8.5 degrees and 11.0 degrees preoperatively, and 3.6 degrees and 4.0 degrees at the final follow-up in men and women, respectively. Significant differences in the preoperative tibiotalar angle and improvement were observed between men and women (preoperative, p = 0.020; improvement, p = 0.014). However, there was no significant difference in the final follow-up tibiotalar angle (p =
Table 3
Radiographic Outcomes of Men and Women Groups

|                                | Men (N = 109 ankles) | Women (N = 86 ankles) | P value* |
|--------------------------------|----------------------|------------------------|----------|
| Tibiotalar angle (deg)†        |                      |                        |          |
| Preoperative                   | 8.5 ± 6.6 (-31.1 to 19.8) | 11.0 ± 6.8 (-32.0 to 18.4) | 0.020    |
| Final follow-up                | 3.6 ± 2.1 (-10.2 to 3.2) | 4.0 ± 2.2 (-10.4 to 3.5) | 0.226    |
| Improvement‡                   | 4.9 ± 6.3 (-4.9 to 24.8) | 7.5 ± 6.5 (-4.2 to 26.8) | 0.014    |

*The independent t test was used to analyze age differences in tibiotalar angle. A p-value of < 0.05 was considered significant.
†The values are given as the mean ± standard deviation, with the range in parentheses. To reduce errors in the mean calculation due to positive (valgus) and negative (varus) values, these values are calculated as absolute values.
‡The improvement are given as the mean difference (preoperative minus final).

Complications and Survivorship

There were 19 ankles with complications in men, 20 ankles in women (Table 4). The overall survivorship rate was 96.1%, at a mean follow-up of 7.5 years. There was no significant difference between the two groups (p = 0.621; log-rank test). Survivorship using Kaplan-Meier curves is shown in Fig. 2.

Table 4
Rate of Complications Associated with Total Ankle Arthroplasty

|                                | Men (N = 109 ankles) | Women (N = 86 ankles) | P value* |
|--------------------------------|----------------------|------------------------|----------|
| Major Complications†           | 11 (10.1%)           | 16 (18.6%)             | 0.087    |
| Deep Infection                 | 1 (0.9%)‡            | -                      | 1.000    |
| Periprosthetic Osteolysis      |                      |                        |          |
| Alone                          | 6 (5.5%)             | 11 (12.8%)             | 0.073    |
| With aseptic Loosening         | -                    | 4 (4.7%)‡              | 0.036    |
| With component subsidence      | 4 (3.7%)‡            | 1 (1.2%)‡              | 0.386    |
| Minor Complication†            | 8 (7.3%)             | 4 (4.7%)               | 0.109    |
| Wound Problem                  | -                    | 1 (1.2%)               | 0.441    |
| Heterotopic Ossification       | 8 (7.3%)             | 3 (3.5%)               | 0.352    |
| Total (no. [%])                | 19 (17.4%)           | 20 (23.3%)             | 0.459    |

*The chi-square or Fisher’s exact test was used to analyze differences in the number of complication. A p-value of < 0.05 was considered significant.
†The values are given as the number of ankles, with the percentage in parentheses.
‡These are failure cases that were revised with an exchange of the metallic component.

There were 10 cases (5.1%) of failure that required exchange of a metallic component, due to deep infection (1 case), osteolysis with aseptic loosening (4 cases), and implant subsidence (5 cases). In the failures, 10 ankles were revised to another TAA or arthrodesis. Seventeen patients with periprosthetic osteolysis alone without loosening or subsidence underwent revision with curettage of
an osteolytic lesion, bone grafting, and polyethylene exchange. In those cases, no further progression of osteolytic lesion was reported. One patients had wound problems, however no one progressed to joint infection, and all healed without further surgical procedures. Three of eleven heterotopic ossification patients underwent resection of ossification due to severe pain. Women had a higher prevalence of complications than men, but there were no significant differences between men and women, except osteolysis with aseptic loosening (p = 0.036).

**Discussion**

The most important aim of TAA is to provide an improved and pain relieved ankle joint. Differences of operative outcomes for TAA between men and women could be expected, since there are differences in bone mineral density (BMD), the prevalence of generalized joint laxity, physical activity, and anatomic variations including alignment of lower extremity and bone size between the genders.[24, 34–38] Thus, the primary purpose of this study was to compare the intermediate-term outcomes of TAA depending on gender difference. In this study, primary outcomes were greatly improved in both groups, but we did not find differences with most patient-reported outcomes, complication rates, and survivorship between the two groups. Consequently, those differences between men and women would not be considered as an affecting factor in the clinical outcomes.

Interestingly, unlike other clinical scores, SF-36 is more likely to have a higher score in men than women. Several studies have demonstrated outcome comparisons between men and women for SF-36 scores of the hip and knee.[23, 25] Cherian et al. analyzed 272 consecutive total knee arthroplasty and reported that the SF-36 PCS was significantly better in men at 7 years of follow-up.[25] Khashan et al. suggested that gender-related analysis resulted in significantly higher scores for men compared to women in SF-36 scores for hip osteoarthritis patients.[23] In regard to knee or hip, men have been reported to score significantly better in the SF-36 test. The activities of daily life have been extensively examined and some studies have reported that men were more tolerant of functional recovery and pain relief, while women on the other hand, tended to perceive their function and pain as more restrictive than they actually were.[22, 39]

In terms of radiographic data, the preoperative tibiotalar angles were worse for women than men.
(Table 3). Since there was a significant difference with tibiotalar angles between men and women before surgery, this was considered to be significantly improved by the process of intra-operative correction. Lee et al. reported that, regardless of preoperative deformity type or degree, if the tibiotalar angle of the ankle was corrected with any ligament imbalance or hindfoot deformity through an additional procedure, the TAA showed good outcomes.[19]

The survivorship rate was not significantly different between men and women at a mean follow-up of 7.5 years (96.4% and 93.4%, respectively) \( (p = 0.621) \) (Fig. 2). Gender had minimal effect on survival rates in TAA, perhaps attributable to the fact that there were no significant differences between the mean age at surgery \( (p = 0.114) \) or failure rates \( (p = 0.752) \) between men and women.

In our data, although not statistically significant, prevalence of osteolysis and its complication was higher in women (16 cases, 18.6%) than in men (10 cases, 9.2%) (Table 4). Men and women are known to have a difference in BMD due to multiple factors including hormonal differences, and we thought these differences may be associated with development of osteolysis with aseptic loosening. Morakis et al. reported that aseptic loosening was associated with a significant decrease of cortical bone and trabecular bone volumetric-BMD.[40] Runolfsdottir et al. suggested that women had lower BMD than men, and a greater increase in BMD reductions with decreasing female hormones.[41] In other words, the BMD difference between men and women suggests that women are more likely to develop aseptic loosening than men. However, gender was not a risk factor or prognostic factor for revision by aseptic loosening in total knee arthroplasty.[42] Therefore, further studies on the relationship between the prevalence of osteolysis with aseptic loosening and bone mineral density are needed.

There were several strengths and weaknesses of our study. Furthermore, a single surgeon performed all TAA using the same prosthesis and underwent a similar rehabilitation treatment. Second, all data were prospectively collected and added to this study. However, there were some limitations. First, the overall mean follow-up duration was 7.5 years. This might not be long enough to include late complications. Second, the sample size of the two groups was relatively small to detect a difference on this general subject. This might have limited our ability to evaluate the influence of baseline and
perioperative characteristics on the outcomes of interest. Finally, this study did not further evaluate objective indicators such as BMD, generalized joint laxity, and whole lower extremity alignment.

Conclusions
In the intermediate-term follow-up, mobile-bearing total ankle arthroplasty showed similarly good clinical and radiographic outcomes in patients with ankle osteoarthritis, regardless of gender differences. These results suggest that gender did not seem affect outcomes of total ankle arthroplasty. Further studies with larger number of sample sizes and long-term follow-up are needed to clarify the effect of gender on outcomes.

Abbreviations
TAA: Total ankle arthroplasty; AOS: Ankle Osteoarthritis scale; AOFAS: American Orthopaedic Foot and Ankle Society; SF-36 PCS: Short Form-36 Physical Component Summary; VAS: Visual Analogue Scale; ROM: Range of motion; BMD: Bone mineral density

Declarations
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Authors' contributions
KBL conceived of the study and participated in its design and coordination, carried out the operations. GWL participated in its design, collection and interpretation of the data. GWL wrote the initial manuscript draft which was then revised appropriately by KBL. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets analysed during the current study are not publicly available due to patient confidentiality.

Ethics approval and consent to participate

This study was approved by Chonnam National University Hospital Institutional Review Board (IRB NO: CNUH-2018-202).

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

The mean preoperative and final follow-up clinical values are shown as bar graphs and the gap between the two values is the improvement value. The error bars indicate standard deviation (AOS, Ankle Osteoarthritis Scale; AOFAS, American Orthopaedic Foot and Ankle Society; SF-36 PCS, Short Form-36 Physical Component Summary; VAS, Visual Analogue Scale) (*significant differences in SF-36 PCS scores between the two groups at the final follow-up).
The Kaplan-Meier curve demonstrates the survivorship of total ankle arthroplasty (195 ankles), when the end point was defined as failure of the prosthesis. The overall survival probability of the implant was 96.1% (96.4% in the men’s group and 93.4% in the women’s group) at the mean follow-up up of 7.5 years (p=0.621).