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Total Ankle Replacement Versus Arthrodesis for End-Stage Ankle Osteoarthritis

A Randomized Controlled Trial

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Background: End-stage ankle osteoarthritis causes severe pain and disability. There are no randomized trials comparing the 2 main surgical treatments: total ankle replacement (TAR) and ankle fusion (AF).

Objective: To determine which treatment is superior in terms of clinical scores and adverse events.

Design: A multicenter, parallel-group, open-label randomized trial. (ISRCTN registry number: 60672307)

Setting: 17 National Health Service trusts across the United Kingdom.

Patients: Patients with end-stage ankle osteoarthritis, aged 50 to 85 years, and suitable for either procedure.

Intervention: Patients were randomly assigned to TAR or AF surgical treatment.

Measurements: The primary outcome was change in Manchester–Oxford Foot Questionnaire walking/standing (MOXFQ-W/S) domain scores between baseline and 52 weeks after surgery. No blinding was possible.

Results: Between 6 March 2015 and 10 January 2019, a total of 303 patients were randomly assigned; mean age was 68 years, and 71% were men. Twenty-one patients withdrew before surgery, and 281 clinical scores were analyzed. At 52 weeks, the mean MOXFQ-W/S scores improved for both groups. The adjusted difference in the change in MOXFQ-W/S scores from baseline was −5.6 (95% CI, −12.5 to 1.4), showing that TAR improved more than AF, but the difference was not considered clinically or statistically significant. The number of adverse events was similar between groups (109 vs. 104), but there were more wound healing issues in the TAR group and more thromboembolic events and nonunion in the AF group. The symptomatic nonunion rate for AF was 7%. A post hoc analysis suggested superiority of fixed-bearing TAR over AF (−11.1 [CI, −19.3 to −2.9]).

Limitation: Only 52-week data; pragmatic design creates heterogeneity of implants and surgical techniques.

Conclusion: Both TAR and AF improve MOXFQ-W/S and had similar clinical scores and number of harms. Total ankle replacement had greater wound healing complications and nerve injuries, whereas AF had greater thromboembolism and nonunion, with a symptomatic nonunion rate of 7%.

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Ankle osteoarthritis causes severe pain and disability and has a similar effect on quality of life as end-stage hip arthritis (1, 2). It is estimated that every year in the United Kingdom at least 29 000 patients with symptomatic ankle osteoarthritis are referred in the National Health Service to specialist foot and ankle surgeons, of whom around 4000 have surgery (3). Most ankle osteoarthritis is the result of previous trauma but can result from long-standing inflammatory arthritis, such as rheumatoid arthritis (4, 5).

See also:

Editorial comment. 1765
Summary for Patients I-36

Web-Only
Supplement

Regardless of cause, end-stage osteoarthritis is defined as a combination of severe, unrelenting symptoms, which are sufficient to make a patient consider surgical intervention; radiologic changes consistent with osteoarthritis; and failure of at least 6 months of nonoperative measures, necessitating a definitive surgical procedure.

Although most patients with ankle arthritis respond to nonoperative treatments, such as weight loss, activity modification, support braces, and analgesia, once the disease has progressed to end-stage osteoarthritis, the main surgical treatments are total ankle replacement (TAR) or ankle arthrodesis (ankle fusion [AF]). Although both TAR and AF have been shown to be effective (6–9), they are very different treatments, with one fusing the bones so that there is no ankle joint movement, and the other replacing the joint with the aim of retaining ankle joint movement. With AF, despite the tibiotalar joint being stiff, the remaining 30 joints in the foot can still move. It is difficult for a patient to know which

treatment is more suitable for them, with most seeking guidance from their surgeon (3). There is a lack of high-quality evidence to guide and inform patient care, and no randomized trials have been published comparing the 2 procedures; hence, we set out to determine whether TAR or AF is superior in terms of clinical effectiveness.

METHODS

Trial Design

TARVA (Total Ankle Replacement Versus Ankle Arthrodesis) is a pragmatic, randomized, multicenter, open-label, superiority trial of patients with end-stage ankle osteoarthritis comparing clinical effectiveness of the 2 existing publicly funded and National Health Service–commissioned treatment options: TAR and AF. The trial was done and reported according to the published protocol (10). The trial was approved by the National Research Ethics Service Committee (London, Bloomsbury 14/LO/0807) and is registered in the International Standard Randomised Controlled Trial Number (ISRCTN) registry (11).

Patients

Patients with end-stage ankle osteoarthritis, aged 50 to 85 years, who the treating surgeon believed to be suitable for either TAR or AF (having considered patient characteristics, including deformity, sources of pain, adjacent joints, stability, bone quality, soft tissue envelope, and neurovascular status) were eligible to join the trial. Patients were recruited with written informed consent between 6 March 2015 and 10 January 2019 by the principal investigators in outpatient clinics at 17 sites in the United Kingdom.

Randomization and Blinding

Treatment allocation was done using an independent web-based randomization service (Sealed Envelope) using minimization incorporating a random element, with an overall probability of 85% that the underrepresented intervention would be selected, to ensure balance in the minimization factors between the randomized groups. Patients were randomly assigned in a 1:1 ratio to either TAR or AF, with 3 minimization factors—surgeon and presence of osteoarthritis in 2 adjacent joints (subtalar and talonavicular) as diagnosed on a preoperative MRI scan.

Patients, surgeons, radiologists, and clinical assessors on the trial could not be blinded because of the nature of the procedures and surgical scars. The surgeons who screened and recruited patients were unaware of the randomization allocation, which occurred after eligibility and consent. All surgeons had adequate experience and training and had done a minimum of 20 independent procedures. All investigators met on a regular basis (both before and during the trial) to discuss and ensure that a consistent selection process was maintained.

Interventions

Total ankle replacement surgeons in the United Kingdom use both 2-component, fixed-bearing and 3-component, mobile-bearing implants (12). The surgical technique followed the standard operative procedure, which briefly involved an anterior approach to the ankle joint, protection of the neurovascular bundle, and bony preparation according to the prosthesis used and its instrumentation guided by intraoperative fluoroscopy as required. All implants used were uncemented.

Ankle fusion was done using the surgeon's usual technique of either arthroscopic-assisted or open AF (8). Briefly, tibial and talar joint surfaces were prepared to bleeding cancellous bone, any deformity correction was addressed, and the surfaces were opposed and held with screws and/or plates as required to ensure that the foot was plantigrade and appropriately positioned.

Outcomes

The primary outcome was the difference between the 2 treatment groups in the change in the Manchester–Oxford Foot Questionnaire walking/standing (MOXFQ-W/S) domain scores (0 to 100, lower scores better) from preoperation to 52 weeks postoperation. The MOXFQ-W/S domain was considered to be the most sensitive domain to assess improvement in foot and ankle conditions (13). Secondary outcomes evaluated the difference between groups in change from preoperative scores for MOXFQ-W/S at 26 weeks; MOXFQ pain and social interaction domains and Foot and Ankle Ability Measure ([FAAM] 0 to 100, higher scores better)–activities of daily living (ADL) and sport subscale scores (only in those who participated in sports) at 26 and 52 weeks; and EuroQol 5-Dimension 5-Level measuring quality of life at 12, 26, and 52 weeks.

Total range of motion from the tibia to the floor was captured using a validated technique (13). All adverse events, serious adverse events, and complications reported from consent to 52 weeks were compared between treatment groups. Secondary outcomes also included health economic outcomes, which will be published separately.

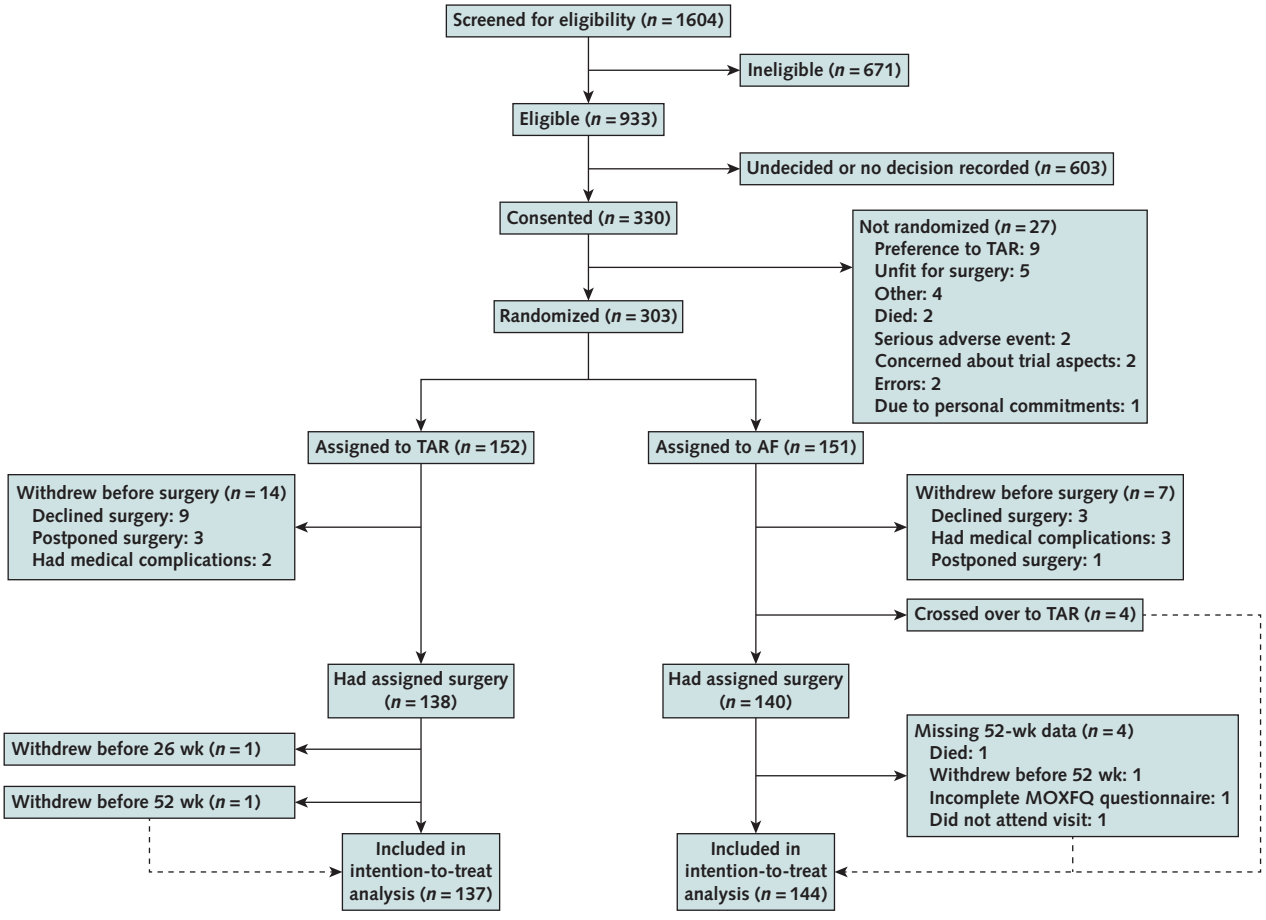
Statistical Analysis

Details of the sample size calculation have been published (14). We estimated that a sample size of 328 patients would be required to detect a minimal clinically important difference of 12 points in the postoperative change in the MOXFQ-W/S domain score between the 2 surgical treatment groups. These calculations were based on a common SD of change from baseline of twenty-seven, 90% power, and an overall type 1 error rate of 5%. In addition, we assumed a surgeon intraclass coefficient of 0.03 and an average of 14 patients per surgeon and allowed for a loss to follow-up rate of 10%.

Effectiveness analyses were done following the intention-to-treat principle where all randomly assigned patients were analyzed according to their randomized surgical procedure. In addition, a per protocol analysis was done for the primary outcome that only included data from patients who received their randomized surgical procedure. All patients for whom data were available at baseline and at least at 26- or 52-week visit were included in the intention-to-treat analysis.

A multilevel, repeated measures, linear regression model was used to estimate the difference between the

Figure. Trial profile (CONSORT [Consolidated Standards of Reporting Trials] diagram).



Of the 282 patients who had surgery, 1 patient who withdrew before 26-week follow-up could not contribute data to the primary outcome but was included in the baseline characteristics table. All 281 patients who had surgery and at least 1 follow-up were included in the mixed model for the primary outcome analysis. AF = ankle fusion; MOXFQ = Manchester–Oxford Foot Questionnaire; TAR = total ankle replacement.

treatment groups in the change in MOXFQ-W/S score from preoperation to 52 weeks after surgery. The model included fixed effects for time, treatment, treatment by time interaction, preoperation MOXFQ-W/S score, and presence of osteoarthritis in each of the 2 adjacent joints (subtalar and talonavicular). A random patient effect and surgeon effect were included to take account of clustering in the data. The model was fitted with an unstructured covariance structure and using restricted maximum likelihood estimation. Secondary outcomes were evaluated using similar mixed models. For the secondary outcomes, point estimates and 95% CIs are reported; these CIs are not adjusted for multiple comparisons. We used STATA/MP, version 15.0 (StataCorp) for all analyses.

A post hoc analysis was done as a sensitivity analysis comparing fixed-bearing TAR and mobile-bearing TAR with AF in a similar model as the primary outcome model.

Role of the Funding Source

The funder had no role in the trial conduct, including data collection, analysis, interpretation, writing of the manuscript, or the decision to submit. The trial was investigator led, and oversight was delivered by a trial management group, supported by independent trial steering and data monitoring committees, as recommended by the funding body (National Institute for Health and Care Research). The trial was sponsored and coordinated by the UCL Comprehensive Clinical Trials Unit.

RESULTS

Patients

A total of 1604 patients were screened, of which 933 were eligible to participate (**Figure**). A total of 152 patients were randomly assigned to TAR and 151 to AF. Of the 303 patients randomly assigned, 21 withdrew from the trial before receiving surgery, 1 withdrew before 26 weeks, and a further 5 patients withdrew or had missing data at week 52. Four patients randomly assigned to AF crossed over to the TAR group. There was a total of 33 surgeons in the trial. The median number of patients per surgeon was 7.

There were more patients with diabetes (11% vs. 7%) and obesity (10% vs. 6%) in the AF group. There were also greater levels of preoperative deformity (greater

Table 1. Baseline Characteristics of Patients Who Had Surgery

Baseline Characteristics	TAR (*n* = 138)	AF (*n* = 144)	Total (*n* = 282)
Mean age (SD), *y*	68.0 (8.1)	67.7 (8.0)	67.9 (8.0)
Sex, *n* (%)			
Female	34 (25)	47 (33)	81 (29)
Male	104 (75)	97 (67)	201 (71)
Mean height (SD), *m*	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)
Mean weight (SD), *kg*	85.8 (13.2)	88.3 (17.4)	87.1 (15.5)
Mean body mass index (SD), *kg/m²*	29.3 (5.9)	30.7 (6.0)	30.0 (6.0)
Smoking status			
Current smoker, *n* (%)	5 (4)	5 (4)	10 (4)
Mean cigarettes/d (SD), *n*	5.8 (2.4)	10.4 (7.4)	8.1 (5.7)
Former smoker, *n* (%)	53 (38)	57 (40)	110 (39)
Mean time since cessation (SD), *y*	25.5 (16.0)	25.9 (15.6)	25.7 (15.7)
Patient treatment preference*, *n* (%)			
No preference expressed	100 (75)	112 (79)	212 (77)
TAR	26 (19)	20 (14)	46 (17)
Arthrodesis	8 (6)	9 (6)	17 (6)
Cause of osteoarthritis, *n* (%)			
Posttraumatic	83 (60)	73 (50)	156 (55)
Primary	46 (33)	56 (38)	102 (36)
Rheumatoid arthritis	6 (4)	7 (5)	13 (5)
Other inflammatory	2 (2)	5 (4)	7 (3)
Other	1 (1)	4 (3)	5 (2)
Presence/absence of osteoarthritis, *n* (%)			
Healthy adjacent joint	81 (59)	79 (55)	160 (57)
Osteoarthritis in subtalar or talonavicular	45 (32)	52 (36)	97 (34)
Osteoarthritis in both adjacent joints	12 (9)	13 (9)	25 (9)
User of assistive device, *n* (%)			
No	80 (58)	79 (55)	159 (56)
Yes†	58 (42)	65 (45)	123 (44)
Medical history, *n* (%)			
Anticoagulants	24 (17)	24 (17)	48 (17)
History of cancer	13 (9)	20 (14)	33 (12)
Chronic pain	40 (29)	46 (32)	86 (31)
Connective tissue disorder	1 (1)	4 (3)	5 (2)
Diabetes	9 (7)	16 (11)	25 (9)
Gastrointestinal disease	17 (12)	22 (15)	39 (14)
Hypertension/hypercholesterolemia	61 (44)	62 (43)	123 (44)
Inflammatory disorder	8 (6)	12 (8)	20 (7)
Metabolic disorder	5 (4)	3 (2)	8 (3)
Neurologic disorder	2 (2)	6 (4)	8 (3)
Obesity	8 (6)	15 (10)	23 (8)
Peripheral nervous system disorder	0 (0)	5 (4)	5 (2)
Peripheral vascular disease	2 (2)	3 (2)	5 (2)
Renal pathology	7 (5)	3 (2)	10 (4)
Respiratory pathology	12 (9)	20 (14)	32 (11)
Thromboembolic disease	7 (5)	7 (5)	14 (5)
Other condition affecting mobility	39 (28)	43 (30)	82 (29)
Degree of deformity, *n* (%)			
16°–30° varus	13 (10)	7 (5)	20 (7)
5°–15° varus	36 (26)	43 (30)	79 (28)
Physiologic neutral	47 (34)	51 (35)	98 (35)
5°–15° valgus	20 (15)	18 (13)	38 (14)
16°–30° valgus	10 (7)	6 (4)	16 (6)
Not available	11 (8)	19 (13)	30 (11)

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Table 1–Continued

Baseline Characteristics	TAR (*n* = 138)	AF (*n* = 144)	Total (*n* = 282)
Fixed flexion deformity of knee, *n* (%)			
No	136 (98.6)	141 (97.9)	277 (98.2)
Yes	2 (1.4)	3 (2.1)	5 (1.8)
Fixed equinus, *n* (%)			
No	131 (94.9)	139 (96.5)	270 (95.7)
Yes	7 (5.1)	5 (3.5)	12 (4.3)
Mean range of motion dorsiflexion (SD), *degree*	14.3 (9.5)	14.2 (9.3)	14.2 (9.4)
Mean range of motion plantarflexion (SD), *degree*	25.4 (8.3)	26.3 (10.5)	25.9 (9.5)
Outcome measures at baseline			
MOXFQ-W/S	81.6 (16.6)	81.5 (16.8)	81.5 (16.7)
MOXFQ–pain	66.7 (16.8)	67.6 (17.5)	67.2 (17.1)
MOXFQ–social interaction	54.4 (26.1)	56.3 (21.7)	55.4 (24.0)
MOXFQ–summary index‡	70.1 (15.4)	70.9 (14.8)	70.5 (15.1)
FAAM-ADL	47.0 (16.7)	44.1 (16.6)	45.5 (16.7)
FAAM–sports	28.3 (19.7)	25.6 (21.3)	27.3 (20.2)
EQ-5D-5L–index value§	0.5 (0.2)	0.5 (0.2)	0.5 (0.2)
EQ-5D-5L–visual analogue scale	72.7 (20.2)	67.5 (21.4)	70.0 (21.0)

AF = ankle fusion; EQ-5D-5L = EuroQol Group 5-Dimension 5-Level; FAAM-ADL = Foot and Ankle Ability Measure–activities of daily living; MOXFQ-W/S = Manchester–Oxford Foot Questionnaire walking/standing; TAR = total ankle replacement.
* Data were missing for 7 participants (4 in TAR and 3 in AF).
† Assistive devices included braces, crutches, walking sticks, and so forth.
‡ Post hoc analysis.
§ EQ-5D-5L-index values were calculated using the mapping function recommended by the National Institute for Health and Care Excellence (15).

than 16° varus or valgus) in the TAR group than in the AF group (17% vs. 9%). Participants were balanced between treatment groups regarding other baseline characteristics, clinical scores, minimization factors, and presence of osteoarthritis in the 2 adjacent joints (Table 1) . Details of the associated procedures, procedure duration, and postoperative immobilization can be found in Supplement Table 1 (available at Annals.org).

The duration of TAR (mean, 121 minutes [SD, 31.6]) was slightly longer than that of AF (mean, 103 minutes [SD, 36.2]). Patients were immobilized for longer in the AF group; 26 (19%) patients were allowed to weight bear within 2 weeks of TAR compared with 7 (5%) in the AF group (Supplement Table 1).

More patients in the TAR group had an associated procedure than in the AF group (35% vs. 18%). The most common procedure was Achilles lengthening, which was done in 17 (12%) patients in the TAR group and 2 (1.5%) in the AF group (Supplement Table 2, available at Annals.org). Six patients (4%) in the TAR group and no patients in the AF group had a lateral ligament repair.

Primary Outcome

Findings for the primary outcome MOXFQ-W/S are in Table 2. The TAR group improved on average by 49.9 points compared with 44.4 points in the AF group, with a mean MOXFQ-W/S domain score at 52 weeks of 31.4 (SD, 30.4) in the TAR group and 36.8 (SD, 30.6) in the AF group. The adjusted difference in the changes from baseline of −5.56 (95% CI, −12.49 to 1.37) suggests that on average patients who received TAR had a greater improvement in MOXFQ-W/S score of 5.56 points compared with AF. This difference was not clinically or statistically significant. Sensitivity analysis done on the per protocol population showed similar findings to that in the intention to treat (Table 2). The results also remained unchanged from the intention-to-treat findings when the primary model was adjusted for differences in preoperative characteristics, which showed differences between groups, including in diabetes, obesity, and greater than 16° of preoperative deformity (Supplement Table 3, available at Annals.org). The same finding was identified when patients with rheumatoid arthritis were excluded from analysis.

Secondary Outcomes

With respect to MOXFQ pain and social interaction domains, patients in both treatment groups improved at 26 and 52 weeks, but there was no clinical or statistically significant difference between TAR and AF. The adjusted difference of −4.20 (CI, −9.80 to 1.39) for pain and −5.06 (CI, −10.37 to 0.26) for social interaction at 52 weeks (Table 3) suggested no difference between groups. The difference between the TAR and AF groups in change in MOXFQ-W/S score at 26 weeks was −8.21 (CI, −15.14 to −1.27). The proportion of patients experiencing the minimum clinically important improvement (14) in MOXFQ-W/S domain of at least 12 points at 52 weeks was similar between the groups–82% of TAR patients versus 80% of AF patients had a clinically relevant improvement in MOXFQ-W/S score.

The FAAM-ADL scores improved in both groups, with greater improvement in the TAR group compared with the AF group at 52 weeks (difference, 6.16 [CI, 1.54 to 10.78]).

Total range of motion in those with TAR improved at 52 weeks from preoperation, whereas it decreased in AF patients.

Adverse Events

Twenty-one percent of randomly assigned patients had at least 1 serious adverse event, including 27 (18%)

patients in the TAR group and 36 (24%) in the AF group. Fifty-four percent of patients had at least 1 adverse event during the trial–82 (54%) patients in the TAR group and 80 (53%) in the AF group.

One patient in the AF group died during the follow-up period, and 1 patient in the TAR group died after the 52-week visit. Both events were unrelated to surgery.

All adverse events and serious adverse events reported during the trial have been summarized as postoperative complications in **Table 4**. There were 20 wound problems in 19 (13%) patients in the TAR group compared with 8 (6%) in the AF group. There were 8 reports of nerve injuries in 6 (4%) patients in the TAR group compared with 1 (<1%) in the AF group. There were 13 thromboembolic events reported in 11 patients–4 (3%) in the TAR group and 7 (5%) in AF group.

Nine (3%) patients–5 in the TAR group and 4 in the AF group–required a further unplanned reoperation other than revision in the 52-week window. One revision in the TAR group occurred within the 52-week window because of a traumatic fall, leading to a periprosthetic fracture and conversion to a tibiotalocalcaneal fusion. In the AF group, 17 (12%) patients did not have plain radiographic evidence of bone union at 52 weeks, but of the 17 patients, only 10 had any symptoms, and hence the symptomatic nonunion rate is 7%. All revisions for nonunion occurred outside of the 52-week window. **Supplement Table 4** (available at Annals.org) lists reoperations and revisions (16, 17).

Prespecified subgroup analysis (**Supplement Figure 1**, available at Annals.org) suggested a greater improvement in MOXFQ-W/S score between TAR and AF when the patients had osteoarthritis in adjacent joints. This difference increased when fixed-bearing TAR was compared with AF (**Supplement Figure 2**, *A*, available at Annals.org).

Of those who received TAR, 54% received fixed-bearing and 46% received mobile-bearing TAR. Of the AF patients, 61% received arthroscopic and 39% received open AF. Overall, all 4 subtypes of patients seemed to be similar with respect to baseline characteristics (**Supplement Table 5**, available at Annals.org) and clinical scores. We did post hoc comparison between the subtypes of TAR patients, those who received fixed-bearing TAR and those who received mobile-bearing TAR, and the AF group (including both open and arthroscopic AF patients). The adjusted difference of −11.1 (CI, −19.3 to −2.9) between fixed-bearing TAR and AF indicates greater improvement in this group compared with AF, but this was not seen in the mobile-bearing TAR group (**Supplement Table 6**, available at Annals.org). The results for open and arthroscopic AF were similar (**Supplement Table 7**, available at Annals.org).

Discussion

This is the first completed multicenter randomized controlled trial to compare TAR with AF for patients with end-stage ankle osteoarthritis. We have not shown superiority of TAR over AF in terms of our chosen clinical score (MOXFQ-W/S domain) at 52 weeks after surgery.

There have been pilot studies (18) and previous attempts at randomized controlled trials, but randomization was an issue leading to a change to cohort studies. A large nonrandomized prospective study of 517 patients was done in which 386 TARs were compared with 93 AFs at 2 years (6). The study showed both treatments to be effective, with an FAAM-ADL score difference between TAR and AF of 9 points (6). This compares favorably with our study, which showed the difference in FAAM-ADL scores between TAR and AF at 52 weeks to be 6.16 (CI, 1.54 to 10.78) in favor of TAR (**Table 3**).

Consistent with our findings, other nonrandomized studies have not shown a difference in clinical scores with follow-up of up to 5 years (7, 8). In addition, a recent systematic review and meta-analysis comparing clinical scores between TAR and AF also reported no statistically significant difference between groups but commented on methodological flaws and heterogeneity of outcome measures (9).

Despite clinically meaningful improvement in the primary outcome measure 52 weeks after surgery in both TAR and AF groups, the adjusted difference in change in MOXFQ-W/S domain scores was not clinically or statistically significant. We believe the MOXFQ to be a highly validated score (13, 19, 20) and the most common used in the United Kingdom; however, there is no global consensus on the ideal outcome measure to use in ankle arthritis (6–9). Nonetheless, we believe this to be the most robust evidence to date that both treatments improve clinical scores but without any discernible difference in clinical scores between the TAR group and the AF group overall at 52 weeks.

Table 2. MOXFQ-W/S at 52 Weeks After Surgery, by Treatment Group

Outcome	TAR			AF			Adjusted Difference in Change From Baseline (95% CI)*†
	Patients, *n*	Mean at 52 Weeks (SD)	Mean Change From Baseline (SD)	Patients, *n*	Mean at 52 Weeks (SD)	Mean Change From Baseline (SD)	
Primary outcome (intention to treat)							
MOXFQ-W/S	136	31.4 (30.4)	−49.9 (30.7)	140	36.8 (30.6)	−44.4 (31.9)	−5.56 (−12.49 to 1.37)
Sensitivity analysis of primary outcome (per protocol)							
MOXFQ-W/S	135	31.4 (30.5)	−49.9 (30.8)	134	36.4 (30.8)	−45.0 (32.4)	−4.84 (−11.96 to 22.8)

AF = ankle fusion; MOXFQ-W/S = Manchester–Oxford Foot Questionnaire walking/standing; TAR = total ankle replacement.
* Adjusted difference is based on 281 patients in the mixed intention-to-treat model who had baseline MOXFQ-W/S score and at least 1 follow-up. Per protocol is based on 269 patients, excluding crossovers and those missing 52-wk visit.
† Adjusted for baseline score of outcomes, presence of osteoarthritis in adjacent joint, and surgeon effect in a mixed-effects model.

Table 3. Secondary Outcomes at 52 Weeks and 26 Weeks, by Treatment Group

Secondary Outcomes	TAR			AF			Adjusted Difference in Change From Baseline (95% CI)*
	Patients, *n*	Mean Value at Follow-up (SD)	Mean Change From Baseline (SD)	Patients, *n*	Mean Value at Follow-up (SD)	Mean Change From Baseline (SD)	
At 52 wk							
MOXFQ-pain	136	26.7 (24.7)	−40.2 (28.0)	140	30.6 (25.7)	−36.7 (24.6)	−4.20 (−9.80 to 1.39)
MOXFQ-social interaction	136	17.0 (20.1)	−37.0 (30.0)	140	22.4 (24.4)	−33.7 (28.0)	−5.06 (−10.37 to 0.26)
MOXFQ-summary index†	136	26.4 (24.5)	−43.7 (26.1)	140	31.2 (25.5)	−39.3 (25.6)	−4.95 (−10.61 to 0.72)
FAAM-ADL	135	81.2 (20.5)	33.8 (22.7)	141	73.8 (20.7)	29.7 (20.7)	6.16 (1.54 to 10.78)
FAAM-sports	37	71.3 (28.8)	41.9 (31.8)	22	75.6 (23.2)	52.7 (26.8)	−4.98 (−18.60 to 8.64)
EQ-5D-5L-index value‡	136	0.7 (0.2)	0.3 (0.3)	140	0.7 (0.2)	0.2 (0.2)	0.02 (−0.02 to 0.07)
EQ-5D-5L-visual analogue scale	136	81.9 (15.2)	9.1 (19.9)	141	77.0 (17.3)	9.4 (22.3)	3.41 (−0.30 to 7.11)
Range of motion–dorsiflexion	132	15.3 (7.2)	1.1 (10.1)	131	9.1 (5.8)	−4.9 (7.9)	6.09 (4.61 to 7.57)
Range of motion–plantarflexion	132	27.3 (7.9)	1.9 (9.8)	131	14.4 (7.2)	−11.7 (11.1)	13.01 (11.24 to 14.77)
At 26 wk							
MOXFQ-W/S	134	35.8 (29.9)	−45.8 (31.0)	141	44.6 (29.6)	−36.9 (31.2)	−8.21 (−15.14 to −1.27)
MOXFQ-pain	134	32.9 (24.3)	−33.8 (25.9)	140	36.2 (24.8)	−31.4 (23.8)	−2.45 (−8.06 to 3.16)
MOXFQ-social interaction	134	22.3 (24.7)	−32.1 (29.5)	140	26.5 (24.4)	−29.6 (26.9)	−3.38 (−8.71 to 1.95)
MOXFQ-summary index†	134	31.5 (25.0)	−38.6 (25.6)	140	37.5 (24.9)	−33.2 (24.9)	−5.13 (−10.80 to 0.55)
FAAM-ADL	132	77.1 (20.0)	30.0 (21.4)	140	70.9 (22.1)	26.8 (21.9)	4.56 (−0.08 to 9.20)
FAAM-sports	39	56.6 (28.1)	27.7 (26.2)	19	62.9 (28.7)	37.3 (35.7)	−7.17 (−21.11 to 6.76)
EQ-5D-5L-index value‡	134	0.7 (0.2)	0.2 (0.2)	141	0.7 (0.2)	0.2 (0.2)	0.04 (−0.004 to 0.09)
EQ-5D-5L-visual analogue scale	134	81.3 (14.8)	8.7 (21.5)	142	76.0 (19.2)	8.1 (22.2)	4.14 (0.43 to 7.85)

AF = ankle fusion; EQ-5D-5L = EuroQol 5-Dimension 5-Level; FAAM-ADL = Foot and Ankle Ability Measure–activities of daily living; MOXFQ-W/S = Manchester–Oxford Foot Questionnaire walking/standing; TAR = total ankle replacement.
* Adjusted for baseline score of outcome, presence of osteoarthritis in adjacent joint, and surgeon effect in a mixed-effects model.
† Post hoc analysis.
‡ EQ-5D-5L–index values were calculated using the mapping function recommended by the National Institute for Health and Care Excellence (15).

Globally, there has been a gradual change in practice of TAR from mobile-bearing implants to fixed-bearing implants. This is in part due to the withdrawal of the most common mobile-bearing implant from the market in 2014, before the onset of recruitment to TARVA. In 2019, more than 70% of implants used in the United Kingdom were of a fixed-bearing type (12). Therefore, we compared the 2 broad types of TAR used in the United Kingdom against AF. In our trial, 54% of TAR patients received a fixed-bearing prosthesis and 46% received a mobile-bearing prosthesis. In a post hoc analysis, we found a statistically significant improvement of fixed-bearing TAR over AF at 52 weeks (adjusted difference, −11.1 [CI, −19.3 to −2.9]), which is close to the minimal clinically important difference of 12 points. Other studies have previously shown potential advantages of fixed-bearing over mobile-bearing ankle implants; this area needs further research (21, 22).

Subgroup analysis modeled for the presence of osteoarthritis in adjacent joints and found the adjusted difference in MOXFQ-W/S was −22.8 (CI, −46.8 to 1.3) between TAR and AF (**Supplement Figure 1**). However, post hoc analysis of the fixed-bearing subtype found that the presence of adjacent joint arthritis favored TAR over AF (adjusted difference, −31.5 [CI, −59.5 to −3.4]) (**Supplement Figure 2**, *A*). This reinforces previous reports that suggest that the presence of adjacent joint arthritis may be an indication for ankle replacement over AF (23). This is especially important because we have shown that 43% of patients had evidence on magnetic resonance imaging of adjacent joint arthritis before their surgery, which is a finding never previously reported. Many of these patients did not have any symptoms in the adjacent joints, but diagnosis of adjacent joint arthritis on magnetic resonance imaging may be an important prognostic indicator between groups with longer-term follow-up.

We did not find a difference between the TAR and AF groups in the risks for having any adverse event; however, there were differences in the types of adverse events, with more wound healing complications (13.8% vs. 5.5%) and nerve injuries (4.3% vs. <1%) in the TAR group than the AF group. There were fewer TAR patients with thromboembolic events—4 (3%) compared with 7 (5%) in the AF group, which may be explained by prolonged immobilization in the AF group. There were no fatal pulmonary embolism events. Our data is important for patient decision making and patient selection. There is sparse comparative data on thromboembolism after ankle surgery, and although the incidence has been reported to be low (24), Hospital Episode Statistics–based studies are subject to confounding because deep venous thrombosis is treated in the outpatient setting, leading to reporting bias. In our study, 98% of patients received some form of thromboprophylaxis; therefore, our data provide pragmatic figures of thromboembolic risk for patients receiving prophylaxis.

Complications after TAR have been classified in terms of risk to implant survival, referring to high-grade complications, such as deep infection; medium grade, such as subsidence; and low grade, such as intraoperative fractures and wound healing issues (15, 25). The higher the grade the more likely implant failure would result. This article provides a comparison of the short-term complications of AF compared with TAR in similar populations that can inform decision making. Long-term outcomes are needed.

Seventeen of 140 (11.8%) AF patients did not have bone union based on plain radiographic review at 52 weeks, but only 6.9% had any symptoms, and hence we report the symptomatic nonunion rate to be 6.9%. Previous estimates of nonunion are between 8% (16) and 10% (26), although it is not always clear from reports whether patients are symptomatic or asymptomatic. In most circumstances, nonunion will be defined by computed tomography scan, and in our series, the diagnosis was made on clinical symptoms coupled with plain radiographs or in some cases computed tomography scans but only where clinically indicated. Although none of the patients in the AF group were revised within the 12-month window, at least 8 of the 17 (47%) nonunited patients are expected to be revised after the 52-week window. Two (12%) are symptomatic but not planning to be revised because of serious comorbidities, and 7 of the 17 (41%) patients were completely asymptomatic and returned to daily activities. Our experience to date supports the finding that surgery for nonunion may not always be required.

Limitations relate to the short-term nature of the follow-up and the pragmatic nature of the study. This is only 52-week data, and longer-term data are essential. There is always a conflict between pragmatic studies and perceived robustness. It could be argued that because surgeons were allowed to use any implant for TAR and any technique for AF that the groups would be too heterogeneous. However, a design whereby surgeons only used 1 type of implant and 1 AF technique would be logistically difficult and far less generalizable. The power of this study was 88%, which was close to our desired power of 90%; we do not believe that the slightly lower power has influenced our conclusions. This study uses the most common implants in the U.K. market, and our data are robust, with a 7% attrition rate, comparing favorably with other orthopedic trials that had attrition rates between 5.3% and 18.2% (27, 28). Further study is needed on cost-effectiveness and the effects of comorbidities on outcomes. Finally, the findings of this study apply to patients whose

Table 4. Adverse Events and Serious Adverse Events, by Treatment*

Safety Outcomes	TAR (*n* = 152), *n*	AF (*n* = 151), *n*	Total (*n* = 303), *n*
Total surgeries (by surgery, not randomization)	142	140	282
Patients experiencing a serious adverse event	27	36	63
Patients experiencing an adverse event	82	80	162
Complication (1–11, higher numbers believed to lead to worse outcome)			
1. Intraoperative bone fracture	3	0	3
2. Wound healing problems†	20	8	28
a. Not requiring antibiotics	3	3	6
b. Requiring antibiotics	17	4	21
c. Requiring debridement	0	1	1
3. Pain undiagnosed	17	23	40
4. Nerve injury	8	1	9
5. Postoperative bone fracture	3	0	3
6. Technical error	0	0	0
7. Reoperation other than revision	5	4	9
8. Bone union issues:	0	17	17
Aseptic loosening for TAR	0	–	0
Nonunion for AF	–	17	17
9. Subsidence	0	0	0
10. Deep infection	0	0	0
11. Implant failure‡	1	0	1
Not related to implant			
Medical complication unrelated to implant (including cardiopulmonary)	73	92	165
Worsening of preexisting musculoskeletal issue	35	35	70
Death	0	1	1
Thromboembolic events			
1. Deep venous thrombosis§	2	5	7
2. Pulmonary embolism§	2	4	6
Other			
Trauma (e.g., falls)	1	3	4
Stiffness	3	1	4
Plaster/immobilization/mobility issues	11	8	19
Tendon complications after surgery	2	2	4
Swelling	8	7	15

AF = ankle fusion; TAR = total ankle replacement.
* Events reported on all 303 randomly assigned patients. Some patients had more than 1 event, and some events were reported more than once.
† In the TAR group, 1 patient had 2 relevant events.
‡ All but 1 revision event occurred after the 52-wk window.
§ In the AF group, 1 patient had both a deep venous thrombosis and pulmonary embolism reported.

surgeon had equipoise over treatment and do not apply to patients that met the exclusion criteria of this study.

In conclusion, both TAR and AF improve patients' MOXFQ-W/S scores at 52 weeks, but overall, neither procedure is superior in terms of clinical scores. Although both operations had similar numbers of adverse events, there is a higher rate of wound healing complications and nerve injuries in the TAR group and a higher rate of thromboembolism in the AF group. The symptomatic nonunion rate for AF was 7%.

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Data Sharing Statement: All data requests should be submitted to the Comprehensive Clinical Trials Unit at UCL at cctu-enquiries@ucl.ac.uk. for consideration. Data that underlie the results presented here will be shared on reasonable request, while preserving patient anonymity. (The complete deidentified patient data set will be made available on publication to researchers whose proposed use of the data has been approved. Requests should be sent to CTU Enquiries at cctu-enquiries@ucl.ac.uk.). The following supporting documents will be made available: study protocol and statistical analysis plan (available at Annals.org).

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Correction: This article was amended on 10 January 2023 to correct errors in the data for "Fixed flexion deformity of knee" and "Fixed equinus" and to add a note regarding missing data in Table 1 and to correct the total number of complications for the intraoperative bone fracture in Table 4. A correction has been published (doi:10.7326/L22-0523).

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