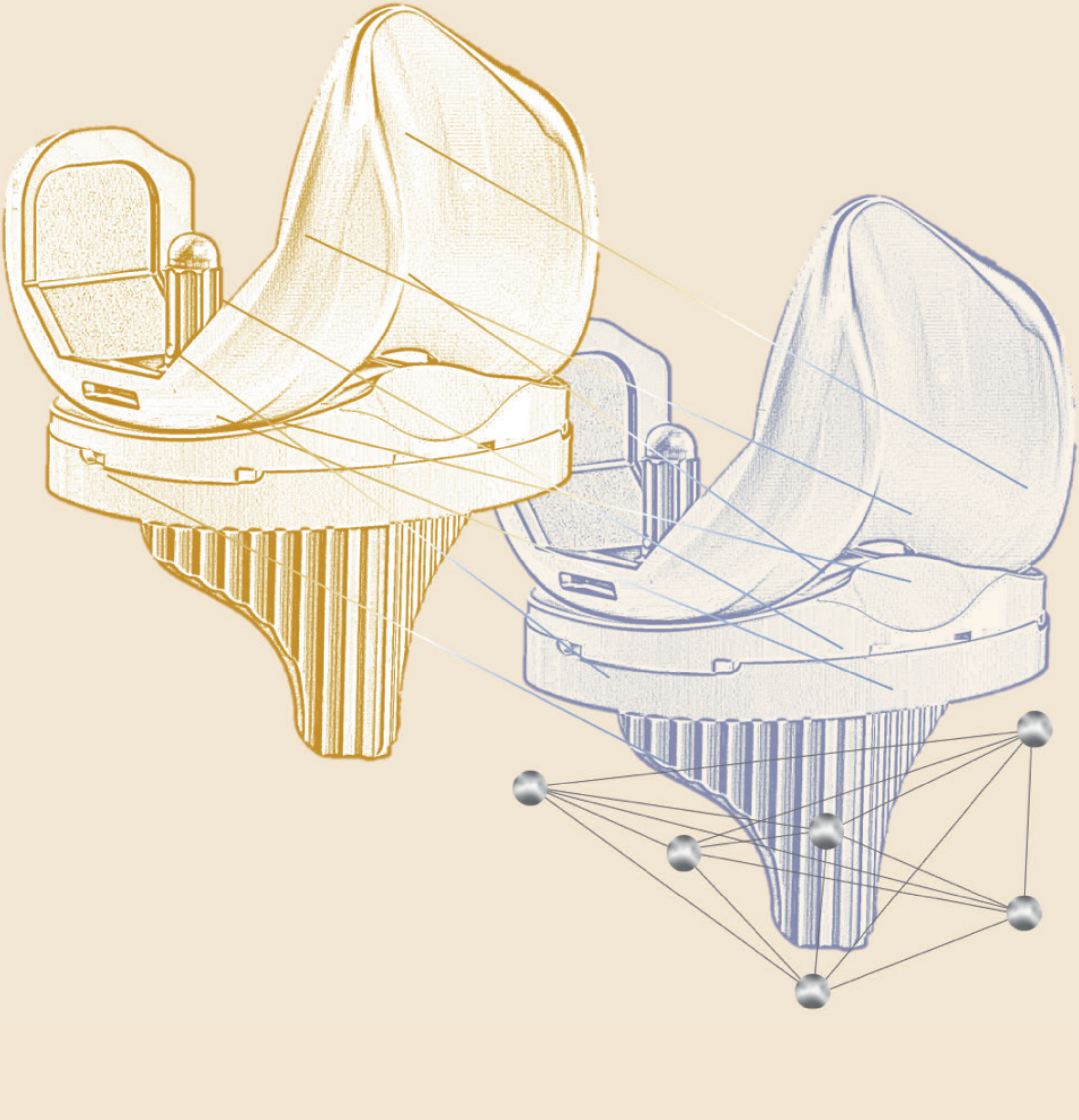
Safety of orthopedic implants: implant migration analysis a must

Hasan, S.



Chapter VIII

The influence of postoperative coronal alignment on tibial migration after total knee arthroplasty in preoperative varus and valgus knees

A secondary analysis of 10 randomized controlled trials using radiostereometric analysis

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Abstract

Background

Orthopaedic surgeons aim for mechanical alignment when performing total knee arthroplasty (TKA) as malalignment is associated with loosening. Loosening may be predicted by migration as measured with radiostereometric analysis (RSA), but previous RSA studies on postoperative alignment have shown contradictory results and have been limited to cemented implants and small numbers of patients. Therefore, we performed a secondary analysis of 10 previously published randomized controlled trials (RCTs) to compare migration between postoperative in-range and out-of-range cemented and uncemented TKA implants among patients with a preoperative varus or valgus knee.

Methods

All RCTs involving the use of RSA that had been conducted at 2 centers were included. Alignment was classified, with use of the hip-knee-ankle angle (HKA), as in-range (0° ± 3°) or out-of-range (<–3° or >3°). The fixation methods included cemented, uncemented-coated, and uncemented-uncoated. Migration was measured at 3, 12, and 24 months. A linear mixed model was used, with adjustment for fixation method and clustering of patients within centers.

Results

Of 476 TKA implants that had been out-of-range preoperatively, 290 were in-range postoperatively and 186 were out-of-range in either varus (n = 143) or valgus (n = 43) postoperatively. The mean migration at 3, 12, and 24 months was 0.73 mm (95% CI, 0.66 to 0.79 mm), 0.92 mm (95% CI, 0.85 to 1.00 mm), and 0.97 mm (95% CI, 0.90 to 1.05 mm), respectively, for the in-range group and 0.80 mm (95% CI, 0.72 to 0.87 mm), 0.98 (95% CI, 0.90 to 1.07 mm), and 1.04 mm (95% CI, 0.95 to 1.13 mm), respectively, for the out-of-range group (p = 0.07). The fixation method significantly

influenced migration, with uncemented-uncoated implants migrating more than cemented and uncemented-coated implants ($p < 0.001$).

Conclusions

Postoperative alignment did not influence migration of TKAs in the first 2 postoperative years in patients with preoperative varus or valgus alignment of the knee. However, the fixation method significantly influenced migration, with uncemented-uncoated implants showing the greatest migration.

Level of Evidence

Level III. See Instructions for Authors for a complete description of levels of evidence.

Background

The debate regarding the optimal coronal alignment of total knee arthroplasty (TKA) implants is ongoing. Traditionally, mechanical alignment as defined as a hip-knee-ankle angle (HKA) of 0° ± 3° (that is, in-range) has been considered the so-called gold standard as studies have shown that malaligned implants are associated with an increased risk of loosening and lower clinical scores.[1,2] Mechanical alignment is considered to be optimal because the weight-bearing load is distributed evenly on the medial and lateral sides of the prosthesis, which in turn reduces wear and loosening.[3,4] However, some patients naturally have some degree of varus or valgus preoperatively[3], and achieving mechanical alignment can be challenging.[5]

The main concern associated with malalignment is the risk of loosening and wear. Loosening can be predicted with radiostereometric analysis (RSA), a highly accurate technique for measuring migration, a factor that has been shown to be associated with the risk of revision TKA.[6-8] Three previous studies assessed the effect of postoperative alignment on migration. Laende et al., in a study of 47 patients who were randomized to mechanical alignment with use of computer-assisted surgery or to kinematic alignment with use of patient-specific instruments, found no difference between the groups in terms of migration or clinical outcomes.[9] Van Hamersveld et al., in a study of 85 TKA implants that had in-range, varus, or valgus alignment postoperatively, found that out-of-range implants, especially those with varus alignment, migrated more than in-range implants.[10] In contrast, Teeter et al., in a small series of 15 TKAs, found no difference in migration between implants with in-range, varus, or valgus postoperative alignment[11]. Besides the limited numbers of patients, those studies included both patients with preoperative neutral alignment and those with preoperative varus or valgus alignment. As achieving postoperative in-range alignment is more straightforward for knees with neutral alignment preoperatively, the influence of failing to achieve mechanical alignment during TKA on migration is of particular interest for patients with preoperative varus or valgus alignment as more releases and larger resections have to be done. Moreover, the above 3 studies were limited to cemented implants. As the interest in uncemented TKA is growing, studies assessing the influence of alignment strategies on migration are needed for both uncemented and cemented implants. Therefore, the aim of the present study was to compare tibial component migration for 2 years postoperatively for TKA implants with in-range or out-of-range (varus or valgus) alignment in patients with preoperative varus or valgus alignment.

Materials and Methods

Design

The present study was a secondary analysis of all randomized controlled trials (RCTs) involving RSA for the analysis of primary TKAs that were performed in the last 2 decades at 2 centers (Hässleholm, Sweden; Leiden, the Netherlands). Ten published RSA studies including 636 patients undergoing TKA from 2002 to 2016 were pooled [Table VIII.I].[12-21] Seven studies were conducted in Hässleholm (432 TKAs)[14-20] and 3 in Leiden (204 TKAs).[12,13,21] Two studies with cemented TKA implants were included in a recently published study on alignment.[10,12,13] One study had 4 treatment arms[12], and 9 studies had 2 treatment arms.[13-21] The number of TKAs per study ranged from 52 to 78. TKA implant designs included cemented, uncemented-coated, and uncemented-uncoated Triathlon implants (Stryker), uncemented-coated Tritanium implants (Stryker), cemented NexGen implants (Zimmer), and cemented Persona implants (Zimmer).

Patients

For a patient to be included in the present study, preoperative and postoperative anteroposterior standing full-leg radiographs, as well as a direct postoperative RSA radiograph and at least 1 RSA radiograph during follow-up, needed to be available for the measurement of alignment. Patients were excluded if

Table VIII.I Study characteristics

Reference	Center	Inclusion period	Number of patients	Implant design	Registration
12	Leiden, The Netherlands	2002-2005	78	NexGen[1] LPS cemented fixed bearing NexGen[1] LPS cemented mobile bearing NexGen[1] LPS High-flexion cemented fixed bearing NexGen[1] LPS High-flexion cemented mobile bearing	Dutch Trial register NTR3287
13	Leiden, The Netherlands	2008-2010	52	Triathlon[2] PS cemented fixed bearing Triathlon[2] PS cemented mobile bearing	ClinicalTrials.gov NCT02924961
14	Hässleholm, Sweden	2006-2006	60	Triathlon[2] CR cemented fixed bearing Triathlon[2] PS cemented fixed bearing	ClinicalTrials.gov NCT00436982
15	Hässleholm, Sweden	2007-2008	60	Triathlon[2] CR uncemented-uncoated fixed bearing Triathlon[2] CR uncemented-coated (PA) fixed bearing	ClinicalTrials.gov NCT03198533
16	Hässleholm, Sweden	2008-2010	60	Triathlon[2] standard-stem CR cemented fixed bearing Triathlon[2] short-stem CR cemented fixed bearing	ClinicalTrials.gov NCT00436982
17	Hässleholm, Sweden	2009-2010	60	Triathlon[2] CR cemented fixed bearing Triathlon[2] CR uncemented-coated (PA) fixed bearing	ClinicalTrials.gov NCT02525601
18	Hässleholm, Sweden	2014-2014	60	Triathlon[2] CR cemented fixed bearing Triathlon[2] CR cemented fixed bearing all-polyethylene	ISRCTN Registry ISRCTN04081530
19	Hässleholm, Sweden	2014-2015	60	Triathlon[2] PS cemented fixed bearing Triathlon[2] PS cemented fixed bearing all-polyethylene	ISRCTN Registry ISRCTN10744502
20	Hässleholm, Sweden	2015-2016	72	Triathlon[2] CR cemented fixed bearing Tritanium Triathlon[2] CR uncemented-coated fixed bearing	ClinicalTrials.gov NCT02578446
21	Leiden, The Netherlands	2014-2015	74	NexGen[1] LPS cemented fixed bearing Persona[1] PS cemented fixed bearing	ClinicalTrials.gov NCT02269254

Table VIII.I Study characteristics. Reference numbers correspond to the reference list. [1]Zimmer Inc, Warsaw, IN, USA; [2]Stryker Inc, Mahwah, NJ, USA. LPS = Legacy posterior stabilizing; PS = posterior stabilizing; CR = Cruciate retaining; PA = Peri-apatite coated;

the knee had a preoperative neutral alignment (an HKA of 0° ± 3°). Age, sex, American Society of Anesthesiologists (ASA) score, body mass index (BMI), Ahlbäck classification, primary diagnosis, and fixation method (cemented, uncemented-coated, or uncemented-uncoated) were collected.

Alignment

Preoperative and postoperative alignment was measured on anteroposterior standing full-leg radiographs in concordance with a standardized protocol; the postoperative radiographs were made at a median of 3 months (interquartile range, 2 to 5 months)[22]In short, the femoral mechanical axis was drawn from the center of the femoral head up to the center of the femoral notch, and the tibial mechanical axis was drawn from the center of the talus up to the center of the tibial plateau. The HKA was the angle between these 2 lines.[10,23] A postoperative HKA of 0° ± 3° was considered in-range, and a postoperative HKA of <–3° (varus) or >3° (valgus) was considered out-of-range. Two observers conducted the measurements regardless of the site. Interobserver variability was assessed by means of measurement of the HKA independently by 2 different observers who were blinded to each other's measurements. The intraclass correlation coefficient (ICC) for measuring the preoperative HKA with use of 208 radiographs was 0.97 (95% confidence interval [CI], 0.96 to 0.97), and the ICC for measuring the postoperative HKA with use of 205 radiographs was 0.94 (95% CI, 0.93 to 0.96). A random set of 44 preoperative and postoperative radiographs was selected to measure intraobserver variability. These double measurements were performed after an interval of 2 months to eliminate the memory effect. In this sample, the ICC for intraobserver variability was 0.96 (95% CI, 0.92 to 0.98) preoperatively and 0.99 (95% CI, 0.98 to 0.99) postoperatively.

Radiostereometric Analysis

The primary outcome of interest was tibial component migration as measured with RSA over a 2-year follow-up period, which is a common follow-up period for RSA studies. RSA radiographs were made within 2 to 3 days postoperatively and at 3 months, 1 year, and 2 years in all studies but one. In that study, RSA radiographs were not made at 3 months and were only made at the other time points.[13] UmRSA software (RSA Biomedical) was used in 4 studies, and Model-Based RSA software (RSACore) was used in 6 studies. Migration was calculated with use of marker-based analysis in 8 studies and model-based analysis in 2 studies. Migration was expressed as the maximum total point motion (MTPM), which estimates the length of the translational vector with the largest migration.[24] As a secondary outcome, implants migrating >0.2 mm in the second postoperative year were considered at risk for early failure.[6] All analyses were performed following the ISO standard and RSA guidelines.[24,25]

Statistics

An independent t test was used for normally distributed continuous variables, and a chi-square test was used for categorical variables, to assess baseline differences. A linear mixed model was used to analyse MTPM over a 2-year follow-up period.[26,27] This model included the group (in-range and out-of-range) and time (baseline, 3 months, 1 year, and 2 years) as fixed effects and an interaction term of group with time. Fixation method (cemented, uncemented-coated, uncemented-uncoated) was included as a fixed effect to adjust for known differences in migration patterns, and the surgical centre (Hässleholm, Leiden) was included as a random effect to account for clustering of patients within these centres. MTPM was log-transformed to obtain a normal distribution. Presented values were back-transformed to the original scale. Remaining variability was modelled with an autoregressive order-1 covariance matrix. As a secondary analysis, the percentage of at-risk implants (an MTPM of >0.2 mm between the 1 and 2-year follow-ups) was compared between both groups with use of a chi-square test.[6] In addition, the out-of-range group was stratified into varus (HKA <–3°) and valgus (HKA >3°) groups, and the primary analysis was repeated. Sensitivity analyses were performed to check whether the results differed if a stricter (HKA 0° ± 1°) or a less strict (HKA 0° ± 6°) threshold was used to classify implants as being in-range. As a post hoc analysis, both the preoperative alignment (that is, varus or valgus) and postoperative alignment (that is, in-range, varus, or valgus) were considered, creating 6 groups (for example, varus-to-valgus alignment). Mean migration was compared between these groups. Means were reported with 95% CIs or standard deviations (SDs), and the level of significance was set at $p < 0.05$. Analyses were performed with use of SPSS statistical software (version 26.0; IBM).

Ethics

All studies were approved by an ethical review board before recruitment of the patients, and all patients provided informed consent. The protocol for pooling of the data was presented to the medical ethics committee of Leiden, who waived the need for approval under Dutch law (P.15.198).

Source of Funding

No funding was received for the current study. Seven of the included studies were funded by Stryker; 2 studies, by the Dutch Arthritis Association; and 1 study, by Zimmer Biomet. The sponsors did not take part in the design, conduct, analysis, or interpretations in the current study.

Figure VIII.I Inclusion Flowchart

RSA = radiostereometric analysis, TKA = total knee arthroplasty, HKA = hip-knee-ankle angle

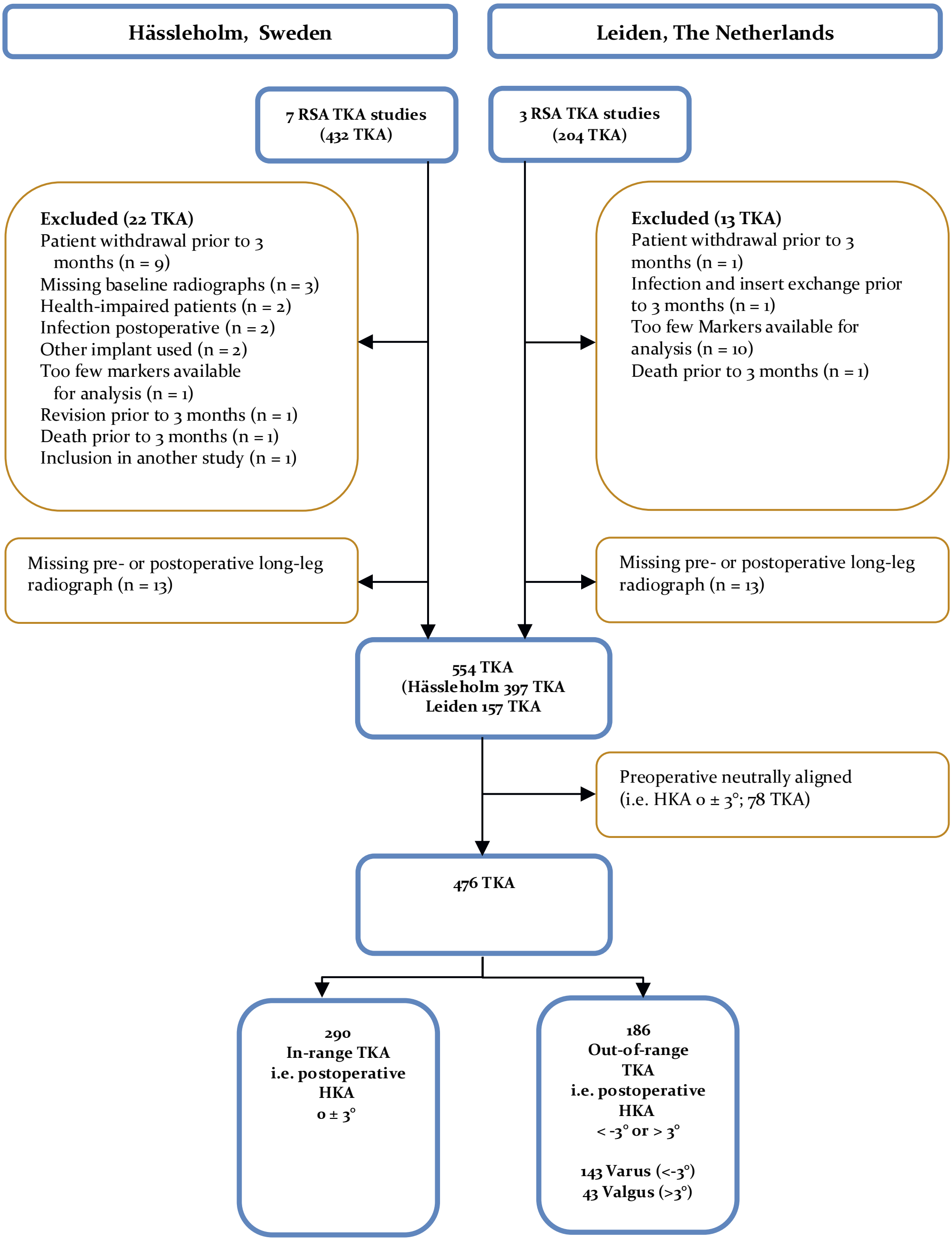

Table VIII.II Baseline characteristics

		Postoperative Hip-Knee-Ankle angle			
		In-range (i.e. HKA 0±3°; n=290)	Out-of-range (i.e. HKA <-3° or >3°; n=186)	p-value	Total (n=476)
Center, n (%)	Hässleholm	229 (79)	123 (66)	0.002	352 (74)
	Leiden	61 (21)	63 (34)		124 (26)
Age, years (SD)		67 (7.3)	67 (8.2)	0.9	67 (8.0)
BMI, kg/m² (SD)		29 (4.4)	29 (4.0)	0.3	29 (4.2)
Sex, n (%)	Female	172 (59)	105 (57)	0.5	277 (58)
	Male	118 (41)	81 (43)		199 (42)
Alignment preop, n (%)	Varus	240 (83)	154 (83)	1.0	394 (83)
	Valgus	50 (17)	32 (17)		82 (17)
Diagnosis, n (%)				0.4	
	Osteoarthritis	269 (93)	171 (92)		440 (93)
	Post-traumatic	1 (0)	0 (0)		1 (0)
	Rheumatoid arthritis*	19 (7)	11 (6)		30 (6)
	Missing	1 (0)	4 (2)		5 (1)
Ahlbäck, n (%)				0.2	
	I	2 (1)	1 (1)		3 (1)
	II	67 (23)	34 (18)		101 (21)
	III	146 (50)	86 (46)		232 (49)
	IV	14 (5)	2 (1)		16 (3)
	Missing	61 (21)	63 (34)		124 (26)
ASA, n (%)				0.3	
	I	59 (20)	37 (20)		96 (20)
	II	193 (67)	129 (69)		322 (68)
	III	36 (12)	16 (9)		52 (11)
	Missing	2 (1)	4 (2)		6 (1)
Fixation, n (%)				0.3	
	Uncemented-	13 (5)	8 (4)		21 (4)
	uncoated	54 (19)	24 (13)		78 (16)
	Uncemented-coated	223 (77)	154 (83)		377 (79)
	Cemented				

*Table VIII.II. Baseline characteristics. HKA = Hip-Knee-Ankle angle. SD = Standard Deviation. Varus: HKA < -3°; Valgus: HKA > 3°. ASA classification = American Society of Anesthesiologists. *Rheumatoid arthritis or another inflammatory disease.*

Results

Of the 636 TKAs that were included in the original 10 RSA studies, 476 TKAs were included in the present study [Fig. VIII.I]. Of these, 290 TKAs were in-range postoperatively (HKA 0° ± 3°) and 186 were out-of-range postoperatively (HKA <–3° [varus, n = 143] or HKA >3° [valgus, n = 43] [Fig. VIII.I]. Relatively more patients underwent the operation in Hässleholm in the in-range group as compared with the out-of-range group (79% compared with 66%; p = 0.002). The primary diagnoses included osteoarthritis (440 knees), rheumatoid arthritis or another inflammatory disease (30 knees), and trauma (1 knee); the diagnosis was missing for remaining 5 knees [Table VIII.II]. The mean postoperative HKA was –1° ± 3.7°, and the median postoperative HKA was also –1° (interquartile range, –3.5° to 0.8°) [Fig. VIII.II].

Figure VIII.II Distribution of the hip-knee-ankle angle

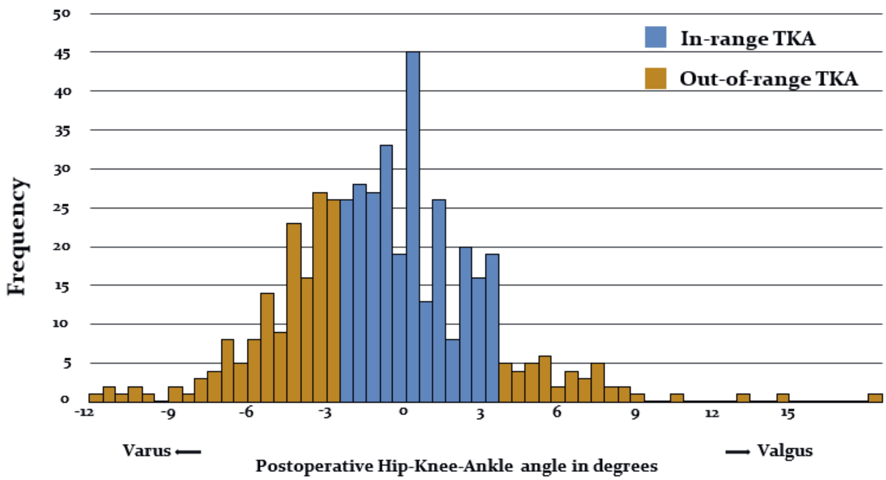

Figure VIII.II Histogram showing the distribution of the postoperative hip-knee-ankle angle (HKA). The blue bars represent the number of in-range TKA implants, and the yellow bars represent the number of out-of-range TKA implants in the primary analysis. An HKA of <–3° is considered varus alignment, and an HKA of >3° is considered valgus alignment. TKA = total knee arthroplasty

No significant difference in MTPM was observed between the alignment groups over the 2-year follow-up period (p = 0.07). The MTPM at 3, 12, and 24 months was 0.73 mm (95% CI, 0.66 to 0.79 mm), 0.92 (95% CI 0.85, to 1.00 mm), and 0.97 mm (95% CI, 0.90 to 1.05 mm), respectively, for the in-range group and 0.80 mm (95% CI, 0.72 to 0.87 mm), 0.98 mm (95% CI, 0.90 to 1.07 mm), and 1.04 mm (95% CI, 0.95 to 1.13 mm), respectively, for the out-of-range group (Fig. VIII.III).

Figure VIII.III Mean migration expressed as the maximum total point motion (MTPM) over time

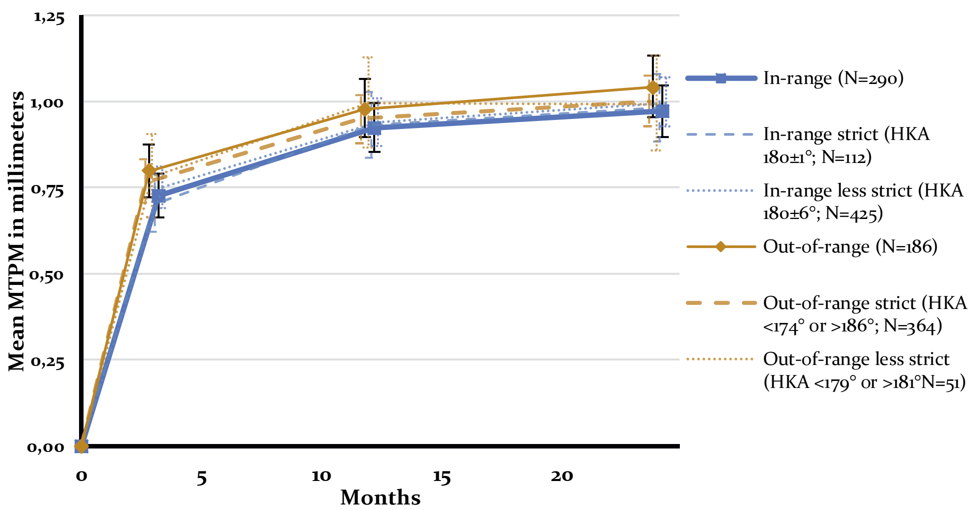

Figure VIII.III. The mean MTPM in millimeters over the 2-year follow-up period labelled by postoperative alignment (In-range: HKA 0 ±3°; Out-of-range: HKA < -3° or > 3°). Error bars represent 95% confidence intervals. The interrupted lines represent the MTPM over time using a strict (i.e. HKA 0 ±1°) or a less strict (i.e. HKA 0 ±6°) threshold to determine TKA in-range and out-of-range. MTPM = Maximum total point motion; HKA = Hip-Knee-Ankle angle; TKA = Total knee arthroplasty

No difference between groups was observed when using a stricter (HKA 0° ± 1°) or less strict (HKA 0° ± 6°) threshold for the classification of in-range (Fig. VIII.III). Similarly, further stratification of the out-of-range group into varus (HKA <–3°) and valgus (HKA >3°) showed no difference between postoperative alignment groups (p = 0.4), including when varus implants were compared with in-range implants (p = 0.08) [Fig. VIII.IV]. The fixation method itself had a significant effect on migration, with uncemented-uncoated implants migrating the most and cemented implants migrating the least (p < 0.001) [Fig. VIII.V]. Both cemented and uncemented-coated implants showed limited migration between 3 months and 2 years [Fig. VIII.V]. The difference in migration between the uncemented-uncoated out-of-range group and

Figure VIII.IV Mean MTPM in a 2-year follow-up period with the out-of-range group subdivided in a varus and valgus group. *The mean MTPM in millimeters over the 2-year follow-up period labelled by postoperative alignment (In-range: HKA 0 ±3°; Varus: HKA < -3°; Valgus: HKA > 3°). The error bars represent 95% confidence intervals.*

MTPM = Maximum total point motion; HKA = Hip-Knee-Ankle angle

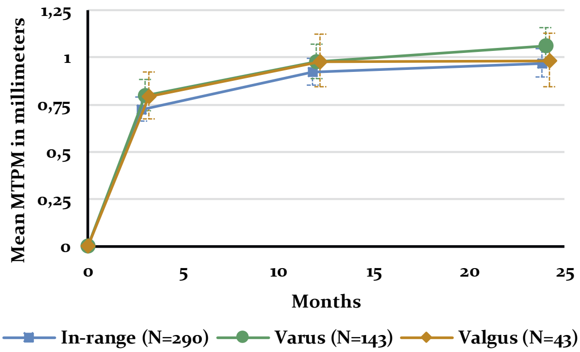

Figure VIII.V Mean MTPM in millimeters over the 2-year follow-up period stratified according to the fixation method

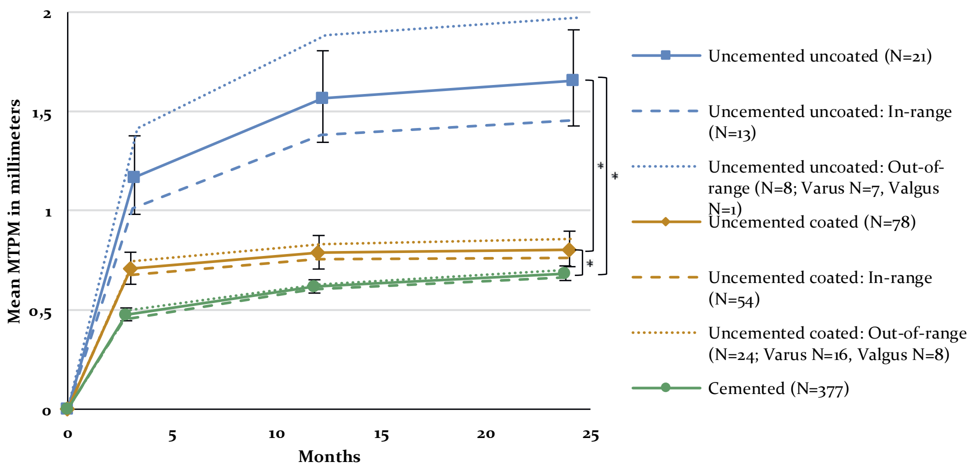

Figure VIII.V. The mean MTPM in millimeters over the 2-year follow-up period stratified by the fixation method of the TKA. The error bars represent 95% confidence intervals. The means are subdivided into an in-range group (i.e. HKA 0 ±3°), and an out-of-range group (i.e. HKA < -3° or > 3°) which are represented by interrupted lines. Statistical significant differences are marked with an asterisk (*). MTPM = Maximum total point motion; HKA = Hip-Knee-Ankle angle

the uncemented-uncoated in-range group did not reach significance as the MTPM at 3, 12, and 24 months was 1.01 mm (95% CI, 0.74 to 1.33 mm), 1.38 mm (95% CI, 1.05 to 1.76 mm), and 1.49 mm (95% CI, 1.14 to 1.90 mm), respectively, for the in-range group and 1.42 mm (95% CI, 1.00 to 1.92 mm), 1.82 mm (95% CI, 1.31 to 2.43 mm), and 1.97 mm (95% CI, 1.46 to 2.59 mm), respectively, for the out-of-range group (p = 0.4) (Fig. VIII.V). Thirty-two implants (13%) in the in-range group and 25 (16%) in the out-of-range group were considered to be at risk for early failure as the migration between the one and two-year follow-up intervals was >0.2 mm (p = 0.3). Stratifying the out-of-range group into varus and valgus groups showed that 22 implants (19%) were at risk for early failure in the varus group and three implants (8%) were at risk for early failure in the valgus group.

The post hoc analysis, including six groups based on preoperative and postoperative alignment (for example, varus-to-valgus alignment), showed that there was a significant difference in migration between groups (p = 0.04) and that patients with preoperative valgus and postoperative varus alignment (that is, valgus-to-varus) had the most migration [Fig. VIII.VI].

Figure VIII.VI Mean migration according to pre- and postoperative alignment

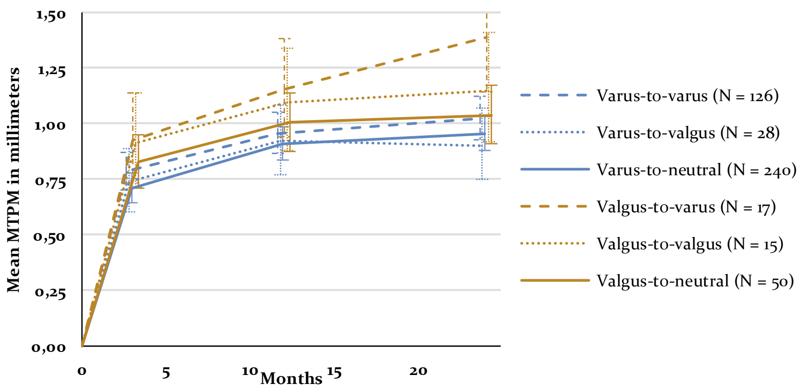

Figure VIII.VI. The mean MTPM in millimeters over the 2-year follow-up period stratified by pre- and postoperative alignment. Varus was defined as an HKA < -3°, valgus as an HKA >3°, and neutral as an HKA 0 ±3°. MTPM = Maximum total point motion; HKA = Hip-Knee-Ankle angle

Chapter VIII

Discussion

The present study of knees with preoperative varus or valgus alignment showed that there was no significant difference between those with postoperative in-range alignment and those with out-of-range alignment in terms of implant migration as measured with RSA during the first 2 postoperative years. The number of implants at risk for early failure was comparable between the groups. These results did not change when stricter or less-strict thresholds were used to define in-range implants or when implants with postoperative varus and valgus alignment were analyzed separately. Post hoc analysis indicated that knees with preoperative valgus alignment that was over-corrected into varus had significantly more migration. In all analyses, the fixation method influenced migration, with uncemented-uncoated implants migrating the most and cemented implants migrating the least. Both cemented and uncemented-coated implants showed limited migration from 3 months onward.

The long-held belief that coronal alignment has a significant influence on results after TKA has been challenged both because the evidence supporting this belief is limited and because studies have demonstrated contradictory results. The results of the present study, which included a larger number of patients than in previous studies, provide further evidence to challenge this belief. This is in line with a case series comparing 7 in-range and 6 varus-aligned TKA implants, which showed no difference in migration at up to 10 years of follow-up.[11] However, another study demonstrated that 29 varus-aligned implants had more migration in comparison with 47 in-range implants over a 5-year period.[10] Likewise, studies comparing survival or clinical outcomes between in-range and out-of-range implants have demonstrated ambiguous results. Rhee et al. found no differences in terms of clinical outcome or survivorship between computer-assisted and conventional TKAs, even though better postoperative alignment with fewer outliers was seen in the computer-assisted group.[28] Several studies have shown no difference between in-range and out-of-range implants in terms of clinical scores or survivorship[29-31], whereas other studies have shown better clinical outcomes for in-range implants.[32,33] Despite these inconsistent findings, much efforts has been put into the development of novel methods to perfectly align implants, such as robot-assisted surgery and patient-specific instrumentation. However, those novel surgical techniques have not resulted in less migration or increased patient satisfaction.[34-36] Future studies should assess whether other factors, such as implant size or bone quality, may be important when considering alignment strategies and migration of TKA implants.

The present study found that uncemented-uncoated implants migrated the most and cemented implants migrated the least. Studies assessing migration for different fixation methods at up to 5 and 10 years have shown comparable results.[37,38] The present study also showed that uncemented-coated implants tended to migrate more initially but were as stable as cemented implants beyond 3 months, which is in agreement with the findings of several studies.[20,39-42] A long-term RSA study comparing different fixation methods suggested that biological fixation of uncemented-coated implants could outperform cemented implants in terms of migration.[43] Those results further strengthen the case for using uncemented-coated TKA implants. The present study adds to that literature indicating that postoperative in-range versus out-of-range alignment does not influence migration of implants at 2 years of follow-up but that it is the fixation method, particularly uncemented-uncoated fixation, that influences migration. Long-term follow-up of the patients in the included studies is needed to address whether postoperative alignment influences migration across a 5 or 10-year period.

To our knowledge, the present study is one of the few multicenter, pooled RSA studies involving the use of individual patient-level data. In most RSA studies, RSA is used to assess the initial migration of a novel implant design as compared with its predecessor. The benefits of using RSA for this purpose are that small groups of approximately 30 patients each are needed, and results become available after 1 or 2 years of follow-up. However, as such studies are powered to compare the migration between 2 groups of specific implants, they are mostly underpowered to answer other clinical questions requiring subgroup analyses. Future studies should consider pooling RSA studies to address such unanswered questions, including the impact of alignment on long-term migration.

Several limitations should be noted. First, all TKA procedures were performed with the intention to achieve mechanical alignment, and reasons why this was not achieved were not registered. Second, preoperative and postoperative anteroposterior standing full-leg radiographs, which were used to define in-range and out-of-range groups, were not made at standardized time points. In theory, the HKA could change preoperatively and postoperatively over time because of progressive osteoarthritis or migration of an implant. Third, although migration was corrected for the originating center and fixation method, there may have been residual confounding due to factors such as osteoporosis if these were distributed differently across the groups. Fourth, migration may depend on implant design, so ideally the impact of alignment would be investigated within the same implant design. Fifth, the group of uncemented-uncoated implants was small (n = 21), which could have resulted in a type-II error as the point estimates of in-range and out-of-range implants seemed different but had large confidence intervals. Finally, the present study assessed migration up to 2 years as a proxy for tibial loosening. Studies assessing the long-term effect of varus or valgus alignment on revision rates are needed before drawing conclusions regarding the longevity of out-of-range TKA implants.

In conclusion, the present study showed that for patients with preoperative varus or valgus knees, postoperative alignment did not influence the mean tibial component migration in the first 2 postoperative years or the number of implants at risk for early loosening. Applying stricter or less-strict thresholds for defining an in-range aligned TKA implant gave similar results. The fixation method significantly influenced implant migration, with uncemented-uncoated implants showing the most migration.

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