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REVIEW ARTICLE

Comparison of Kinematic Alignment and Mechanical Alignment in Total Knee Arthroplasty: A Meta-analysis of Randomized Controlled Clinical Trials

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The aim of this study was to estimate whether kinematic alignment (KA) improves knee function or clinical outcomes compared with mechanical alignment (MA) in the short term after total knee arthroplasty (TKA). We searched the literature for randomized controlled trials published before January 2020 from PubMed, EMBASE, Google, Web of Science, Cochrane Library, and other databases. The observation markers included "The Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index," "Knee Society Score (KSS)," "Oxford Knee Score (OKS)," "combined Knee Society Score (KSS)," "Knee injury and Osteoarthritis Outcome Score (KOOS)," "European Quality of Life Measure-5 Domain-5-Level (EQ-5D-5L)," range of motion (ROM), lower limb alignment, ligament release, and complications. A total of 11 randomized controlled trial studies were included in the study. During the follow-up of 6–24 months, the KA-TKA group was superior to the MA-TKA group in terms of WOMAC scores, combined KSS, KSS, knee function scores, and knee range of flexion, but there was no significant difference in EQ-5D-5L, KOOS, KOOS (symptoms, pain, ADL, sports, and quality of life), complications, knee range of extension, hip-knee-ankle (HKA) angle, tibial component slope angle, lateral distal femoral angle (LDFA) or medial proximal tibial angle (MPTA) angle between the MA-TKA group and the MA-TKA group (P > 0.05). Our meta-analysis revealed that the incidence of ligament release in the MA-TKA group was higher than that in the KA-TKA group. This meta-analysis shows that the KA-TKA group had better clinical outcomes and knee range of flexion than the MA-TKA group at short-term follow-up.

Key words: Alignment; Knee joint; Meta-analysis; Total knee arthroplasty

Introduction

O steoarthritis (OA) is the most widespread joint disease in the elderly, and knee osteoarthritis (KOA) is more frequent than OA of the hip or ankle^{1, 2}. It has been predicted that in 2020, OA will be the fourth most common cause of disability worldwide³. At present, the first choice for severe joint diseases (Kellgren–Lawrence score \geq 3) is total knee arthroplasty (TKA), which can relieve joint pain, correct deformity, and improve joint function, and many studies have suggested that the long-term survival rate could reach more than 90% after 15 years^{4–6}. It has been estimated that by 2030, every year, 3.8 mn people will undergo TKA⁷. Although the survival rate of TKA has improved, approximately 20%-25% of patients remain unsatisfied with the outcome⁸.

Traditional mechanical alignment (MA) has been used in TKA for more than 30 years, and it is still common worldwide. It is generally believed that a hip-knee-ankle (HKA) angle within less than 3° of the neutral mechanical axis is essential for postoperative limb recovery after TKA^{9, 10}. With the development of knee biomechanics, however, many people have assumed that MA does not entirely restore normal lower limb alignment, may alter the normal kinematics of knee motion and so contribute to some of the most serious ramifications. Some foreign scholars¹¹⁻¹³ have found that the kinetic characteristics of the normal knee are

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Orthopaedic Surgery 2020;12:1567-1578 • DOI: 10.1111/os.12826

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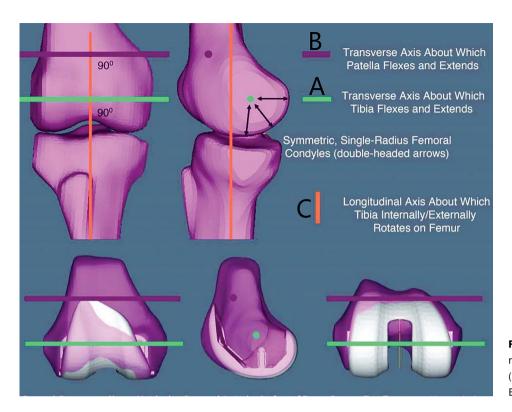


Fig. 1 The kinetic characteristics of normal knee are governed by three axes. (Photo credit: Dossett HG, Swartz GJ, Estrada NA. *et al.*¹³

governed by three axes (Fig. 1). One is the transverse axis of the femur; during knee flexion and extension, the tibia moves around the transverse axis of the centerline of the medial and lateral condyle of the femur¹⁴⁻¹⁶. Another is the patellar transverse axis, a transverse axis around which the patella rotates during knee flexion and extension; its spatial position is anterior and proximal of the central transverse axis of the femur^{17, 18}. The last axis is the longitudinal axis of the tibia, which is perpendicular to the transverse axis of the femur; the tibia rotates internally and externally around the longitudinal axis of the tibia¹⁶⁻¹⁸. Therefore, the overall mechanical alignment takes into account the twodimensional alignment of the parts with the center of the femoral head, knee, and ankle. Kinematic alignment (KA) is different from mechanical alignment (MA) in that it mainly considers the three-dimensional alignment of the components relative to the knee and involving movement in 6° of freedom (6-DOF: front-to-back, proximal-to-distal, internally-to-externally, extension-to-flexion, varus-to-valgus, internal-to-external rotation)^{12, 13}. Based on this theory, in 2006, Howell et al.¹⁹ proposed kinematic alignment in TKA (KA-TKA). The primary purpose of KA-TKA is to control the kinematics of the patella and tibia relative to the femur by restoring the above mentioned three axes of the distal femur and the proximal tibia rather than merely generating a neutral HKA angle.¹² Meanwhile, Howell et al.¹² also proposed an osteotomy and guide apparatus customized for KA-TKA patients. However, this technique requires a highly reliable method. In other words, pre-operative threedimensional scans of the articular surface of the femoral and tibia by MRI, in an MRI scan, require flexion-extension axis (FEA) of tibia vertically to the sagittal. In addition to this, manual instrument techniques were also reported to be effective²⁰. But, the following important aspects should be carefully evaluated: line of force of the lower limbs; anatomic axis of the knee; internal-external rotation of the tibia component relative to the femur; valgus or varus degrees placement of the tibia component; anatomic axis of the knee²¹. Howell et al.²² tested two methods for this purpose, and found that the accuracy was similar with and without Patient Specific Cutting Blocks. Some studies^{19, 23-27} have shown that KA-TKA is more likely to restore normal knee kinematics and that its clinical outcome is guite favorable compared with MA-TKA. And they consistently concluded that KA-TKA could significantly improve patient's quality of life, higher mean flexion range angle, and reduced the prevalence of pain, joint stiffness, and instability²⁸. However, KA-TKA has some potential problems: an increased risk of patellar instability and polyethylene wear^{29, 30}.

While relevant meta-analyses have been published in recent years, these studies included randomized controlled trials, case reports, and systematic reviews^{27, 31}. Two systematic reviewss^{27, 31} have analyzed the kinematic and mechanical alignment techniques in TKA. These two meta-analysess^{27, 31} included retrospective observational studies and randomized controlled trials (RCTs). Both authors agree that the KA-TKA provided better functional outcomes in addressing pain and improving function. Waterson *et al.*³²

have also analyzed 71 KOA patients undergoing TKA in which 36 patients underwent kinematic alignment treatment and 35 patients received mechanical alignment. The results showed that the two groups had similar function 1year postoperatively. Another recent randomized controlled trial showed that the KA-TKA offered better pain relief and higher mean flexion range angle than the MA-TKA at two years³³. As the quality of data in these studies is often limited, differences in results exist. It is still uncertain whether the benefits of KA-TKA are superior to those of MA-TKA. Therefore, we systemically analyzed the available data after searching the literature for randomized controlled trials to evaluate whether the clinical outcome of KA-TKA is better than that of MA-TKA.

Materials and Methods

Search Strategy

This meta-analysis method was based on the Cochrane Collaboration standard. We searched the literature database for randomized controlled trials (RCTs) published before January 2020. The databases that were searched included PubMed, EMBASE, Google, Web of Science, and Cochrane Library. The retrieval strategy was performed by the method of free words combined with the Medical Subject Headings (MeSH). The literature search was conducted using the keywords "Total Knee Arthroplasty," "Kinematic Alignment," "Kinematic," "Mechanical Alignment," "Mechanical," and "biomarker" using Boolean operators (AND), (OR), and (NOT). Literature was retrieved without restricting the language.

Inclusion and Exclusion Criteria

Criteria for inclusion: (i) randomized controlled trials; (ii) comparisons of clinical results between KA-TKA and MA-TKA in total knee arthroplasty; (iii) primary knee replacement surgery; (iv) observation indexes include "The Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index,", "Knee Society Score (KSS),""Oxford Knee Score (OKS)," "combined Knee Society Score (KSS)," "Knee injury and Osteoarthritis Outcome Score (KOOS)," "EQ-5D-5L," range of motion (ROM), lower limb alignment, ligament release, and complications; and v) studies published in English.

Criteria for exclusion: (i) basic research or cadaver study; and (ii) inaccessible data or full-text.

Data Extraction

Data from the studies from all selected articles were extracted independently by two of the authors using a data extraction template, which was designed before the database searches. From each study, first author, years, type of study and surgery, sample size, follow-up time, and clinical outcome were extracted from the literature. Any disagreement was resolved through discussion and consensus or consultation with other authors in cases of disagreement. If the data KINEMATIC ALIGNMENT IN TOTAL KNEE ARTHROPLASTY

from a study was missing, insufficient, or vague, we contacted the author or corresponding authors by email or telephone to retrieve further information.

Quality Evaluation

Literature quality was evaluated independently by two of the authors with the Cochrane Collaboration Network risk

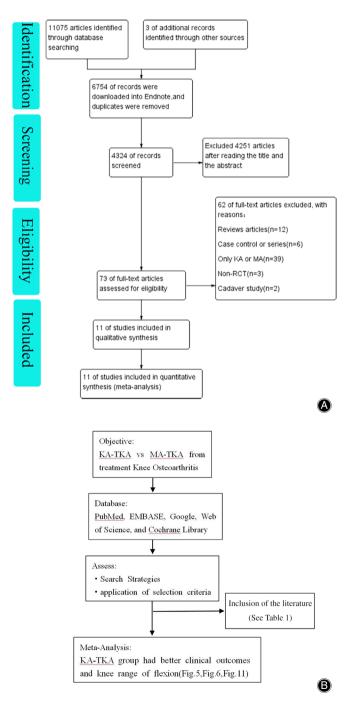


Fig. 2 (A) Flow chart of literature processing. (B) The literature guide search and results.

evaluation tool. The risk of bias for each indicator was divided into three levels: "low," "high," and "unclear." If we obtained more than 10 articles, a funnel chart or Eggers regression test was used to assess publication bias.

Observation Indexes

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

The WOMAC is a validated questionnaire to evaluate lower extremity osteoarthritis and joint replacement. The WOMAC questionnaire produces three subscale scores (pain, stiffness, and physical function) and a total score. Patients are asked to answer each question about the severity of pain, stiffness, or behavioral difficulties experienced in the previous 48 hours. There are five response options ranging from "none" to "extreme" to choose. A response of "none" was scored as 0,"mild" as 1, "moderate" as 2, "severe" as 3, and "extreme" as 4. The scores of the questions in each subscale were summed together to get scores for pain, stiffness, and physical function. A lower subscale score indicates less pain, less stiffness, or better physical function. A total score of < 70 is considered a severe score, 21–48 is moderate, <21 is mild.

Knee Society Score (KSS)

The KSS is a condition-specific validated questionnaire widely used to evaluate the functional capabilities of the knee joint before and after total knee arthroplasty. The scoring

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system consists of two parts. One part is the knee score. The assessment includes pain (maximum 50 points), stability (maximum 25 points), total range of flexion (maximum 25 points), and other items (varus, valgus, extension delay, and flexion contracture). The other part is the function score. The assessment includes walking distance (maximum 50 points), ability to climb stairs (maximum 50 points), and the use of walking aids. The highest score for each part is 100 points, and a higher score means better knee function. The evaluation result score is rated as four levels: 80–100 points, 70–79 points, 60–69 points, <60 points.

Statistical Analysis

Statistical analysis of all extracted data was carried out using Review Manager 5.3 (The Cochrane Collaboration, Oxford, UK), with P < 0.05 considered statistically significant. Heterogeneity between studies was evaluated by calculating the I^2 . If the I^2 was greater than 50%, it was considered high heterogeneity, and a random-effects model was chosen to analyze the data; otherwise, the fixed-effects model was applied. Enumerated data were presented as the risk ratio (*RR*) or odds ratio (*OR*) and 95%*CI*, while continuous data were presented as the weighted mean difference (*WMD*) or standardized mean difference (*SMD*) and 95%*CI* as a statistical measure of the curative effect. We attempted to use a funnel plot to evaluate the publication bias; a symmetrical funnel plot may indicate a low publication bias, while an asymmetric funnel plot may indicate possible publication bias.

Authors		o	T	Sample	size (knees)	- - - -	Measurement index
	Year	Study design	Total patients	KA	MA	Follow-up times (months)	
MacDessi et al. ³⁴	2020	RCT	128	70	68	12	Operative time, FJS-12, KOOS, HKA angle, LDFA, MPTA, KOOS, EQ-5D-5L
McEwen et al. ³⁵	2020	RCT	82	41	41	24	Tibial component slope angle, Femoral rotation angle, Ligament release,KOOS,OKS,FJS-12,HKA angle, LDFA, MPTA, Extension/Flexion range
Yeo et al. ³⁶	2019	RCT	60	30	30	8.0 years	WOMAC, KSS, Flexion range
Laende et al. ³⁷	2019	RCT	47	24	23	24	Ligament release, UCLA, OKS, HKA angle, MPTA
Young et al. ³⁸	2017	RCT	99	49	50	24	Tibial component slope angle, Femoral rotation angle, Ligament release,WOMAC,KSS,OKS,FJS-12 HKA angle,LDFA,MPTA,EQ-5D-5L,Flexion range
Calliess et al. ³⁹	2017	RCT	200	100	100	12	Tibial component slope angle, WOMAC, KSS, HKA angle, LDFA, MPTA
Waterson et al. ³²	2016	RCT	86	36	35	12	KSS,UCLA,KOOS,EQ-5D-5L,Flexion range
Dossett et al. ³³	2014	RCT	120	60	60	24	WOMAC,KSS,OKS,HKA angle,LDFA,MPTA, Extension/Flexion range
Matsumoto et al. ⁴¹	2017	RCT	60	30	30	12	KSS,Extension/Flexion range
Dossett et al. ¹³	2012	RCT	120	41	41	6	Operative time, WOMAC, KSS, OKS, HKA angle, Extension/Flexion range
Claudio et al. ⁴⁰	2015	RCT	144	72	72	6	KSS

FJS-12, Forgotten Joint Score-12; LDFA, Lateral distal femoral angle; MPTA, Medial proximal tibial angle; UCLA, University of California, Los Angeles Activity Score.

Results

Literature Search Results and Study Characteristics

We retrieved 11,075 papers from the databases; 6754 duplicates were removed by EndNote X9.1 software (Fig. 2). This left 4324 articles. Next, 4251 articles were excluded after reading the titles and abstracts, and the remaining 73 articles were retained for further evaluation by reading the full texts. Of these articles, 11 randomized controlled trials (RCTs)^{13, ³²⁻⁴¹ were included, with a total of 553 patients in the KA-TKA group and 550 patients in the MA-TKA group. The literature guide search and results are shown in Fig. 2B. The basic information of the 11 included articles is shown in Table 1.}

Risk-of-bias and Publication Bias Assessment

The 11 papers included were evaluated for risk of bias according to the seven aspects in Fig. 3, which shows that all the RCT articles had a low risk of bias. The symmetrical funnel plot may indicate low publication bias (Fig. 4).

Clinical Outcomes

Five randomized controlled trials^{13, 33, 36, 38, 39} with a total of 599 patients evaluated WOMAC scores. We detected high heterogeneity between the KA-TKA and MA-TKA groups $(I^2 = 93\%)$. We found that one of these studies³⁶ reported the results in the long term (8-year follow-up), while other studies reported a short-term follow-up. We excluded this article from our meta-analysis for further analysis. The meta-analysis result was heterogeneous $(I^2 = 71\%)$, so the random-effects model was used for further analysis. The results showed that the WOMAC score of the MA-TKA group was higher than that of the KA-TKA group [MD = -10.60, 95% CI (-16.17, -5.04), P = 0.0002, Fig. 5].

Knee joint function and pain scores were evaluated by the KSS and OKS. The total knee scores of the KA-TKA group were better than those of the MA-TKA group, and the differences were statistically significant [$I^2 = 74\%$, MD = 10.13, 95% CI (5.76, 14.50), P < 0.00001, Fig. 6]. Three trials with a total of 402 patients evaluated the combined KSS. The random-effects model was used instead of a fixed-effects model due to the high heterogeneity ($I^2 = 84\%$) of the combined KSS. The combined KSSs were better in the KA-TKA group than in the MA-TKA group, and the difference between the groups reached statistical significance [MD = 18.10, 95% CI (8.90, 27.30), P = 0.0001, Fig. 6].

Two trials^{36, 38} with a total of 238 patients evaluated the KSS. The results indicated that the mean scores of the KA-TKA group were higher than those of the MA-TKA group [MD = 11.52, 95%*CI* (6.58, 16.45), P < 0.00001, Fig. 6]. Six trials^{13, 33, 36, 38, 40} with a total of 565 patients evaluated the knee function score. According to the different scoring times, 6 months^{13, 40} and 12–24 months,^{33, 36, 38} the included studies were divided into two subgroup analyses. Two trials^{13, 40} followed up 226 enrolled patients for 6 months, and based on our findings, the KA-TKA group had higher mean

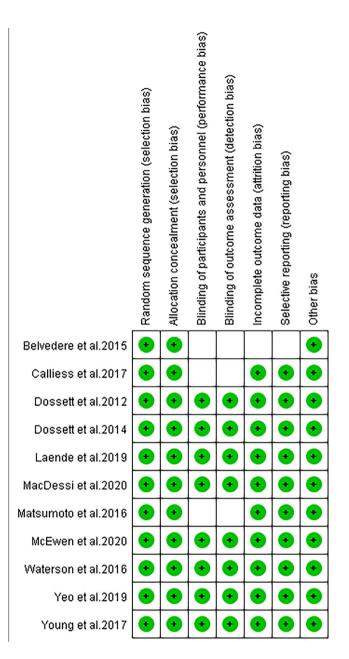


Fig 3 . Eleven articles underwent Risk-of-Bias Assessment summary.

scores than the MA-TKA group [MD = 11.36, 95% CI (6.20, 16.51), P < 0.0001, Fig. 6]. Four trials^{33, 36, 38} followed up 339 enrolled patients for 12–24 months, and the results showed that the two groups had similar mean scores [MD = 3.93, 95% CI (-2.79, 110.65), P = 0.25, Fig. 6]. Five trials^{13, 33, 35, 37, 38} with a total of 430 patients evaluated OKS. However, one study¹³ calculated the scores differently from the others, and hence, we excluded this article from this study. The meta-analysis result was heterogeneous $(I^2 = 69\%)$, so the random-effects model was used for further analysis. The results showed that the two groups had similar

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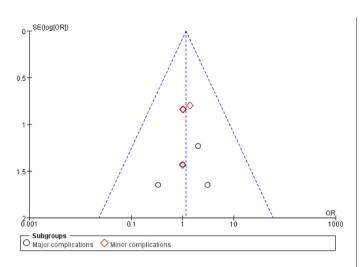


Fig. 4 The funnel plot for the symmetrical may indicate a low publication bias.

mean scores [MD = 2.05, 95%CI (-0.59, 4.68), P = 0.13, Fig. 7].

Quality of life (QoL) was evaluated using KOOS and EQ-5D-5L. Three trials with a total of 291 patients evaluated KOOS. The meta-analysis result showed low heterogeneity $(I^2 = 0\%)$, and hence, a fixed-effects model was used for further analysis. Figure 8 shows that these two groups had similar mean scores in terms of KOOS [MD = 1.83, 95%CI (-1.72, 5.38), P = 0.31], KOOS symptoms [MD = 1.58, 95%]CI (-1.97, 5.12), P = 0.38], KOOS pain [MD = 1.34, 95%CI(-2.66, 5.35), P = 0.51, KOOS ADL [MD = 0.89, 95% CI(-2.38, 4.16), P = 0.59], KOOS sports [MD = 2.71, 95%CI(-4.45, 9.87), P = 0.46], and KOOS QoL [MD = 1.83, 95%CI (-2.76, 56.58), P = 0.42]. Three trials with a total of 291 patients evaluated EQ-5D-5L. The meta-analysis result showed low heterogeneity ($I^2 = 0\%$), and hence, a fixedeffects model was used for further analysis. The results showed that the two groups had similar mean scores [MD = 0.53, 95% CI (-2.86, 3.92), P = 0.76, Fig. 9].

Lower Limb Alignment

Basic lower limb alignment measurements should include the HKA angle, tibial component slope angle, femoral component rotation to sulcus line angle, LDFA, and MPTA KINEMATIC ALIGNMENT IN TOTAL KNEE ARTHROPLASTY

angle. The random-effects model was used instead of a fixedeffects model since there was heterogeneity. Figure 10 shows that the two groups had similar mean scores in terms of HKA angle [$I^2 = 83\%$, MD = -0.29, 95%*CI* (-1.13, 0.55), P = 0.50], tibial component slope angle [$I^2 = 92\%$, MD = 0.85, 95%*CI* (-0.86, 2.56), P = 0.22], LDFA angle [$I^2 = 97\%$, MD = -0.54, 95%*CI* (-2.36, 1.27), P = 0.38], and MPTA angle [$I^2 = 96\%$, MD = 0.94, 95%*CI* (-2.43, 0.55), P = 0.22]. The results of two trials with 181 patients showed that the femoral component internal rotation to sulcus line angles of the two groups were different [$I^2 = 0\%$, MD = -2.16, 95%*CI* (-2.92, -1.39), P < 0.00001, Fig. 10]. From the data in Fig. 8, the rotation angle of the KA-TKA group still had a varus alignment, whereas the MA-TKA group presented with a valgus pattern.

ROM

Our review found a total of seven relevant studies, including four studies^{13, 33, 35} involving extension range angle and seven studies involving flexion range angle^{13, 32, 33, 35, 36, 38}. As seen from Fig. 11, the difference in extension range angle did not reach statistical significance $[I^2 = 1\%, MD = -0.45, 95\% CI (-1.01, 0.12), P = 0.12]$ but the difference in flexion range angle did $[I^2 = 59\%, MD = 3.14, 95\% CI (1.37, 4.91), P = 0.0005]$. Furthermore, the KA-TKA group had a higher mean flexion range angle than the MA-TKA group (P = 0.0005).

Ligament Release and Complications

Three articles^{35, 37, 38} with 228 enrolled patients reported ligament release. Intraoperatively, 77 cases of ligament releases were recorded, with 29 cases in the KA-TKA group and 48 cases in the MA-TKA group. The fixed-effects model was used instead of a random-effects model due to the low heterogeneity ($I^2 = 0\%$). The incidence of ligament release was lower in the KA-TKA group than in the MA-TKA group [MD = 0.28, 95% CI (0.13, 0.59), P = 0.0008, Fig. 12].

Of the 11 studies, five studies^{13, 33, 35, 38, 39} provided data regarding complications (KA-TKA: 15/582; MA-TKA: 13/584). There was no statistical significance between the two groups ($I^2 = 0\%$, MD = 1.16, 95%CI (0.55, 2.41), P = 0.70, Fig. 13). All the complications were clustered into two subgroups: subgroup 1 (major complications) and subgroup 2 (minor complications). Figure 13 shows that these two groups had the same result in terms of major

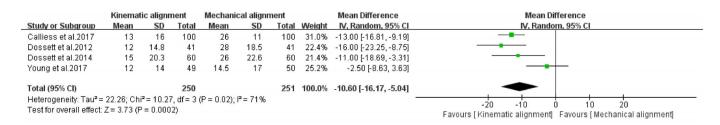


Fig. 5 The forest plot for WOMAC (0–96 best-worst).

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	Kinemat	tic alignn	nent	Mechani	cal alignn	nent		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
1.2.1 KSS(Combined)									
Calliess et al.2017	190	18	100	178	17	100	11.2%	12.00 [7.15, 16.85]	-
Dossett et al.2012	174	31.3	41	149	35.3	41	5.4%	25.00 [10.56, 39.44]	
Dossett et al.2014	160	31.9	60	137	37.9	60	6.3%	23.00 [10.47, 35.53]	
Subtotal (95% CI)			201			201	22.9%	18.10 [8.90, 27.30]	
Heterogeneity: Tau ² = 38	.97; Chi ² =	4.82, df	= 2 (P =	0.09); I ² =	58%				
Test for overall effect: Z =	3.86 (P =	0.0001)							
1.2.2 KSS (Society)									
Dossett et al.2012	90	14.3	41	79	18.2	41	9.7%	11.00 [3.92, 18.08]	
Dossett et al.2014	84	17.1	60	72	21.1	60	9.8%	12.00 [5.13, 18.87]	
Subtotal (95% CI)			101			101	19.5%	11.52 [6.58, 16.45]	◆
Heterogeneity: Tau ² = 0.0	00; Chi ² =	0.04, df=	= 1 (P = 0	0.84); I ² = 0	%				
Test for overall effect: Z =	4.58 (P <	0.00001)						
1.2.3 KSS (function,follo	w 6month	1)							
Belvedere et al.2015	90	15	72	80	23	72	10.2%	10.00 [3.66, 16.34]	
Dossett et al.2012	84	19.9	41	70	21	41	8.5%	14.00 [5.14, 22.86]	
Subtotal (95% CI)			113			113	18.7%	11.36 [6.20, 16.51]	◆
Heterogeneity: Tau ² = 0.0	00; Chi ² =	0.52, df=	= 1 (P = 0	0.47); l ² = 0	%				
Test for overall effect: Z =	4.32 (P <	0.0001)							
1.2.4 KSS (function,follo	w 12-24m	ionth)							
Dossett et al.2014	77	19.2	60	65	21.1	60	9.6%	12.00 [4.78, 19.22]	
Matsumoto et al.2016	68.3	13.6	30	64	15.9	30	9.4%	4.30 [-3.19, 11.79]	
Yeo et al.2019	90.1	10.5	30	93	9.1	30	11.1%	-2.90 [-7.87, 2.07]	
Young et al.2017	83	18	49	79.5	24	50	8.8%	3.50 [-4.85, 11.85]	
Subtotal (95% CI)			169			170	38.9%	3.93 [-2.79, 10.65]	◆
Heterogeneity: Tau ² = 34	.24; Chi ² =	= 11.46, c	df = 3 (P =	= 0.009); P	²= 74%				
Test for overall effect: Z =	1.15 (P =	0.25)							
Total (95% CI)			584			585	100.0%	10.13 [5.76, 14.50]	◆
Heterogeneity: Tau ² = 38	.27: Chi ⁼=	= 39.01. d	df = 10 (F	• < 0.0001); I ² = 74%			-	
									-50 -25 0 25 50
Test for overall effect: Z =	: 4.54 (P <	0.00001)						Favours [Mechanical alignment] Favours [Kinematic alignment]

Fig. 6 The forest plot for Combined Knee Society score (KSS, 0–200 worst–best), Knee Society Score(0–100 worst–best), Knee function Score (0–100 worst–best).

complications $[I^2 = 0\%, MD = 1.26, 95\%CI (0.33,4.75), P = 0.73]$ and minor complications $[I^2 = 0\%, MD = 1.11, 95\%CI (0.46,2.56), P = 2.70].$

Discussion

Results on the Meta-Analysis

The 11 studies (RCTs) that fulfilled the inclusion criteria included 1103 participants: 553 patients in the KA-TKA group and 550 patients in the MA-TKA group. Furthermore, follow-up ranged from 6 months–8 years. Most of the literature reported that the patients were followed up for 6–24 months. The results of the KA-TKA group were better than those of the MA-TKA group in terms of the WOMAC score, combined KSS, KSS, knee function score, and knee

range of flexion, while the EQ-5D-5L, KOOS, KOOS (symptoms, pain, ADL, sports, and QoL), complications, knee range of extension, HKA angle, tibial component slope angle, LDFA, and MPTA angle in the KA-TKA group were not significantly different from those in the MA-TKA group. The incidence of ligament release in the KA-TKA (29/144) group was lower than that in the MA-TKA (48/144) group, and the difference was statistically significant.

Functional Outcome After KA-TKA

Although the survival rate and the clinical and functional outcomes of TKA are very good overall, approximately 20%–25% of patients remain unsatisfied with the outcome⁸. There are undoubtedly many reasons, but the two main reasons are as follows. (i) Reports have indicated that 98% of normal

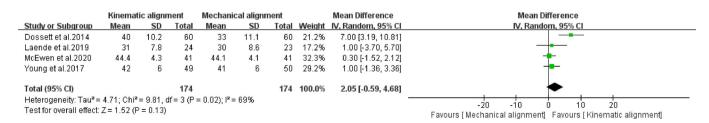


Fig. 7 The forest plot for Oxford Knee Score(0-48 worst-best).

KINEMATIC ALIGNMENT IN TOTAL KNEE ARTHROPLASTY

		tic alignr			cal alignr			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
1.4.1 KOOS									
MacDessi et al.2020	82.2	16.4	70	79.6	14.7	68	9.7%	2.60 [-2.59, 7.79]	
McEwen et al.2020	89.6	12.9	41	88.5	13.7	41	7.9%	1.10 [-4.66, 6.86]	
Waterson et al.2016	77.7	20	36	76.4	19	35	3.2%	1.30 [-7.77, 10.37]	
Subtotal (95% CI)			147			144	20.9%	1.83 [-1.72, 5.38]	•
Heterogeneity: Chi ² = 0	.16, df = 2	(P = 0.92)	2); I ² = 0%	5					
Test for overall effect: Z	C= 1.01 (P	= 0.31)							
1.4.2 KOOS Symptoms	5								
MacDessi et al.2020	80.5	16.5	70	77	14.6	68	9.7%	3.50 [-1.69, 8.69]	+
McEwen et al.2020	89.1	11.3	41	89.2	11.1	41	11.2%	-0.10 [-4.95, 4.75]	
Subtotal (95% CI)			111			109	20.9%	1.58 [-1.97, 5.12]	•
Heterogeneity: Chi ² = 0	.99, df = 1	(P = 0.32)	2); I ² = 0%						
Test for overall effect: Z									
1.4.3 KOOS Pain									
MacDessi et al.2020	86.7	16.1	70	85.4	16	68	9.2%	1.30 [-4.06, 6.66]	- +-
McEwen et al.2020	93.3	13	41	91.9	14.8	41	7.2%	1.40 [-4.63, 7.43]	- <u>t</u>
Subtotal (95% CI)			111			109	16.4%	1.34 [-2.66, 5.35]	◆
Heterogeneity: Chi² = 0	.00, df = 1	(P = 0.98)	3); I ² = 0%						
Test for overall effect: Z	= 0.66 (P	= 0.51)							
1.4.4 KOOS ADL									
MacDessi et al.2020	86.5	15.2	70	84.5	16.4	68	9.4%	2.00 [-3.28, 7.28]	
McEwen et al.2020	93.7	9.3	41	93.5	9.9	41	15.2%	0.20 [-3.96, 4.36]	- <u>+</u> -
Subtotal (95% CI)			111			109	24.6%	0.89 [-2.38, 4.16]	+
Heterogeneity: Chi ² = 0	.28, df = 1	(P = 0.60)); I ² = 0%	5					
Test for overall effect: Z									
1.4.5 KOOS Sports									
MacDessi et al.2020	62.3	25.4	70	57.4	29.1	68	3.2%	4.90 [-4.22, 14.02]	
McEwen et al.2020	61.5	25	41	62.3	28.3	41	2.0%	-0.80 [-12.36, 10.76]	
Subtotal (95% CI)			111			109	5.1%	2.71 [-4.45, 9.87]	*
Heterogeneity: Chi ² = 0	58 df=1	(P = 0.4)		,					-
Test for overall effect: Z			<i>,</i> ,,, = 0 ,						
1.4.6 KOOS QoL									
MacDessi et al.2020	75.1	22.6	70	71.5	21.8	68	4.8%	3.60 [-3.81, 11.01]	-+
McEwen et al.2020	85.8	13.9	41	85	13.9	41	7.3%	0.80 [-5.22, 6.82]	_ _
Subtotal (95% CI)			111			109	12.1%	1.91 [-2.76, 6.58]	*
Heterogeneity: Chi ² = 0	33. df = 1	(P = 0.57)							
Test for overall effect: 2			,,, _ 0,						
Total (95% CI)			702			689	100.0%	1.52 [-0.10, 3.14]	•
Heterogeneity: Chi ² = 2	64 df = 1	2 (P = 1 f		%				,,	
Test for overall effect: Z				~					-50 -25 0 25 50
									Favours [Kinematic alignment] Favours [Mechanical alignment]

Fig. 8 The forest plot for knee injury and osteoarthritis score (KOOS, 0-100 worst-best).

limb femoral and tibial mechanical axes are not in a straight line and that 76% of normal limbs exceed the range of 3° of the neutral mechanical axis¹⁶. Bellemans *et al.*⁴² studied 250 young adults without arthritis and showed that the rate of constitutional varus knees was 24.6%, with a rate of 32.0% for males and 17.0% for females. If these patients need to be treated by MA-TKA, the clinical outcomes of patients will still be poor after surgery. (ii) MA-TKA does not entirely restore knee joint kinematics, kinetic characteristics can irritate the soft tissue, and imbalance of the knee joint has attracted the full attention of domestic and foreign scholars. The proposed kinematic alignment is based on the concept of the kinematic axes of the knee and their relationship to the femoral condyles^{14, 15}. KA-TKA does not restore the HKA angle of the limb to neutral, it mainly considers the three-dimensional alignment of the components relative to the knee, which may lower the frequency of ligament release and improve clinical effectiveness^{19, 36–38}. Recently, two RCTs compared KA *vs* MA in TKA, and KA-TKA reduced the incidence of ligament release^{35, 37}. Our meta-analysis revealed that the rate of ligament release in MA-TKA was higher than that in KA-TKA (P = 0.0008). Consistent with findings in previous studies^{27, 31, 33, 36, 38–40}, we found that the KA-TKA group had better knee function outcomes than the MA-TKA group in terms of the WOMAC score, KSS, combined KSS, and KSS.

Complications and Survival

Although the goal of KA-TKA is to restore normal knee kinematics or prearthritic kinematics and restore the patient

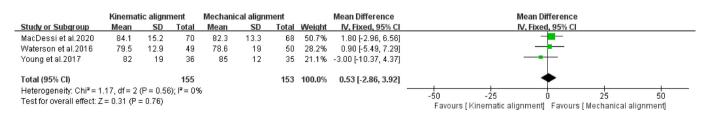


Fig. 9 The forest plot for EQ-5D-5L.

KINEMATIC ALIGNMENT IN TOTAL KNEE ARTHROPLASTY

	Kinemat			Mechanic				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
.6.1 HKA angle									
Calliess et al.2017	-1	3	100	1	1	100	4.5%	-2.00 [-2.62, -1.38]	
Dossett et al.2012	0.3	2.8	41	0	2.2	41	4.2%	0.30 [-0.79, 1.39]	
Dossett et al.2014	0.1	2.8	60	-0.1	2.5	60	4.3%	0.20 [-0.75, 1.15]	
Laende et al.2019	-2.3	2.6	24	-2.1	2.1	23	4.0%	-0.20 [-1.55, 1.15]	
MacDessi et al.2020	-0.2	2.3	70	-0.6	2.3	68	4.4%	0.40 [-0.37, 1.17]	_+
McEwen et al.2020	-0.2	2.4	41	-0.2	2.1	41	4.4%	-0.80 [-1.78, 0.18]	
	-0.4	2.4	49	-0.2	2.1	50	4.2%		
Young et al.2017	-0.4	3	385	-0.7	2	383	4.2%	0.30 [-0.71, 1.31]	
Subtotal (95% CI)	04. OF 7						29.9%	-0.29 [-1.13, 0.55]	
Heterogeneity: Tau ² = 1			п= 6 (P	< 0.00001);	r= 83%	•			
Test for overall effect: Z	= 0.67 (P =	= 0.50)							
1.6.2 LDFA angle									
Calliess et al.2017	88	1	100	89	0	100		Not estimable	
Dossett et al.2014	88.7	2	60	90.8	2.7	60	4.4%	-2.10 [-2.95, -1.25]	
MacDessi et al.2020	89.2	1.8	70	90.6	1.5	68	4.5%	-1.40 [-1.95, -0.85]	
McEwen et al.2020	91.8	2	41	89.9	0.6	41	4.5%	1.90 [1.26, 2.54]	
Yeo et al.2019	87.5	1.7	30	90.1	0.4	30	4.5%	-2.60 [-3.22, -1.98]	
Young et al.2017	92	2.5	49	90.5	1.6	50	4.4%	1.50 [0.67, 2.33]	
Subtotal (95% CI)			350			349	22.3%	-0.54 [-2.36, 1.27]	
Heterogeneity: Tau ² = 4	16: Chi ² =	142.67		<pre>< 0 00001</pre>	$1^{\circ} I^{2} = 97^{\circ}$				
Test for overall effect: Z			ui - 4 (i	0.00001	// - 51	~			
	0.00 (0.00)							
1.6.3 MPTA angle									
Calliess et al.2017	88	1	100	89	0	100		Not estimable	
Dossett et al.2014	90.2	2.6	60	90	2.1	60	4.4%	0.20 [-0.65, 1.05]	
Laende et al.2019	86.7	2	24	89.2	1.7	23	4.2%	-2.50 [-3.56, -1.44]	
MacDessi et al.2020	88.9	1.83	70	90	1.9	68	4.5%	-1.10 [-1.72, -0.48]	
McEwen et al.2020	87.5	1.3	41	89.7	0.4	41	4.6%	-2.20 [-2.62, -1.78]	
Yeo et al.2019	91.7	1.9	30	89.5	0.4	30	4.5%	2.20 [1.51, 2.89]	
Young et al.2017	87	3	49	89.3	1.8	50	4.3%	-2.30 [-3.28, -1.32]	
Subtotal (95% CI)			374			372	26.4%	-0.94 [-2.43, 0.55]	
Heterogeneity: Tau² = 3	1.30; Chi ² =	135.04,	df = 5 (F	P ≤ 0.00001); l² = 96'	%			
Test for overall effect: Z	= 1.24 (P :	= 0.22)							
1.6.4 Tibial component									
Calliess et al.2017	4	3.4	100	4	2	100	4.4%	0.00 [-0.77, 0.77]	
McEwen et al.2020	3.1	1.8	41	3.2	1.8	41	4.4%	-0.10 [-0.88, 0.68]	
Young et al.2017	4	2.5	49	1.3	2	50	4.3%	2.70 [1.81, 3.59]	
Subtotal (95% CI)			190			191	13.2%	0.85 [-0.86, 2.56]	
Heterogeneity: Tau ² = 2	.11; Chi ² =	26.47, d	f=2 (P	< 0.00001);	I [≥] = 92%				
Test for overall effect: Z	= 0.98 (P =	= 0.33)							
1.6.5 Femoral rotation									
McEwen et al.2020	-1.3	3.1	41	1.1	2.5	41	4.1%	-2.40 [-3.62, -1.18]	<u> </u>
Young et al.2017	-0.5	2.5	49	1.5	2.5	50	4.3%	-2.00 [-2.98, -1.02]	
Subtotal (95% CI)			90			91	8.3%	-2.16 [-2.92, -1.39]	◆
Heterogeneity: Tau ² = 0	100° Chi ^z =	0.25 df	= 1 (P =	0.62): $P = 0$	196				
Test for overall effect: Z				0.02/,1 = 0	~~~				
TOTAL OF OVERALL ENGLY, Z	- 0.02 (F	0.0000	·/						
Total (95% CI)			1389			1386	100.0%	-0.52 [-1.20, 0.17]	
Heterogeneity: Tau ² = 2	R1: Chiz-	207.07		مەمە م ح	13:12 - 0		100.070	-0.32 [-1.20, 0.17]	
neterouenenty, rau ⁺ = 2			ui = 22 (, ~ 0.0000	17.1.= 8	4 /0			-4 -2 0 2 4
Test for overall effect: Z									

Fig. 10 The forest plot for HKA, LDFA, MPTA, tibial component slope and femoral rotation angle.

	Kinemat	tic alignn	nent	Mechani	cal alignn	nent		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
1.9.1 Extension range	(°)								
Dossett et al.2012	0.7	1.7	41	0.8	2.2	41	40.3%	-0.10 [-0.95, 0.75]	
Dossett et al.2014	2	3.8	60	3	3.8	60	15.8%	-1.00 [-2.36, 0.36]	
Matsumoto et al.2016	-2	3.1	30	-0.8	1.9	30	17.2%	-1.20 [-2.50, 0.10]	
McEwen et al.2020	0	3	41	0	3	41	17.3%	0.00 [-1.30, 1.30]	
Subtotal (95% CI)			172			172	90.7%	-0.45 [-1.01, 0.12]	•
Heterogeneity: Chi ² = 3.1	02, df = 3 (i	P = 0.39)	; I ² = 1%						
Test for overall effect: Z =	= 1.54 (P =	0.12)							
4.0.2 Flavian Danse (8)									
1.9.2 Flexion Range (°)				445	40.0	17	4.000	5 00 10 00 0 7 01	
Dossett et al.2012	120	9.2	41	115	12.3	41	1.3%	5.00 [0.30, 9.70]	
Dossett et al.2014	121	10.4	60	113	12.5	60	1.7%	8.00 [3.89, 12.11]	
Matsumoto et al.2016	122.3	8.9	30	116.8	12.6	30	1.0%	5.50 [-0.02, 11.02]	
McEwen et al.2020	127	10	41	127	11	41	1.4%	0.00 [-4.55, 4.55]	
Waterson et al.2016	120	9.5	36	118.4	9.4	35	1.5%	1.60 [-2.80, 6.00]	
Yeo et al.2019	125	11.5	30	129	11.5	30	0.9%	-4.00 [-9.82, 1.82]	
Young et al.2017	119	11	49	116	11	50	1.6%	3.00 [-1.33, 7.33]	
Subtotal (95% CI)			287			287	9.3%	3.14 [1.37, 4.91]	-
Heterogeneity: Chi ² = 14	4.75, df = 6	(P = 0.02)	2); I ² = 59	3%					
Test for overall effect: Z =	= 3.48 (P =	0.0005)							
Total (95% CI)			459			459	100.0%	-0.11 [-0.65, 0.43]	•
Heterogeneity: Chi ² = 32	2 08 df = 10	0 (P = 0 (- 69%		400		0.11[-0.00] 0.40]	
Test for overall effect: Z:			5004), 1	- 00 /0					-10 -5 0 5 10
Test for subaroup differe			. df = 1 (P = 0.0002). I² = 93.0)%			Favours [Mechanical Alignment] Favours [Kinematic Aigment]

Fig. 11 The forest plot for extension/flexion range of knee.

KINEMATIC ALIGNMENT IN TOTAL KNEE ARTHROPLASTY

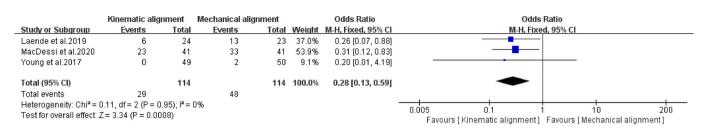


Fig. 12 The forest plot for ligament release.

to previous functional levels, the concern for increased risk of patellofemoral instability and polyethylene wear was raised^{29, 30, 43-45}. Ishikawa *et al.*⁴⁶ found that patients with more significant femoral rollback and external rotation of the femur can obtain better restoration of the motion of tibia flexion-extension after KA-TKA. Our updated meta-analysis found that the KA-TKA group had a higher mean flexion range angle than the MA-TKA group (P = 0.0005). However, Ishikawa et al.46 expressed concern about varus alignment of the tibial prosthesis, which can increase the risk of polyethylene wear, leading to reduced prosthesis survival, and which also increases contact stress at the patellofemoral joint and may cause patellofemoral joint instability. Our meta-analysis reported three patients with patellar instability: two patients in the KA-TKA group^{13, 38} and one patient in the MA-TKA group³⁸. The results showed that the two groups had similar rates of complications (KA-TKA: 15/582, MA-TKA: 13/584, P = 0.70). Howell *et al.*²⁴ prospectively followed 214 knees subjected to KA-TKA, and the mean follow-up was 38 months (31–43 months). There has been great interest in

investigating varus (>3°) or valgus (<-3°) knee alignment, and there was no polyethylene wear or loosening leading to loosening of the revision prosthesis in comparison with alignment of the HKA angle in range $(0^{\circ} \pm 3^{\circ})$. Another study showed that after patients underwent the KA-TKA, 80% presented with varus alignment of the tibial component, and 70% had a varus alignment of the limb. However, varus alignment of the tibial component and limb did not adversely affect implant survival or function during the follow-up periods. Of the patients whose follow-up was 3 to 8 years (mean, 6.3 years), only two cases of loosening of the prosthesis were considered failures; the survival rate was 97.5% and the revision rate was 0.4%⁴⁷. Howell *et al.*⁴⁸ show that the overall survival rate of prostheses hold on pleasurable, the 10-years survival rate of approximately 97.5%. Yeo et al.36 reported the follow-up of patients after KA-TKA and MA-TKA for 8 years, and they obtained similar clinical and radiological results. Thus, they suggested that the increased risk of surgical failure after KA-TKA may not hold. However, KA-TKA as a new option for the treatment of patients

	Kinematic alig	nment	Mechanical alignm	ient		Odds Ratio	Odds Ratio	
Study or Subgroup	Events	Total			Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	
2.2.1 Major complicat	tions							
Calliess et al.2017	2	100	1	100	7.4%	2.02 [0.18, 22.65]		
Dossett et al.2012	0	41	0	41		Not estimable		
Dossett et al.2014	1	60	1	60	7.4%	1.00 [0.06, 16.37]		
McEwen et al.2020	1	41	0	41	3.6%	3.07 [0.12, 77.69]		
Young et al.2017	0	49	1	50	11.1%	0.33 [0.01, 8.38]		
Subtotal (95% CI)		291		292	29.6%	1.26 [0.33, 4.75]		
Total events	4		3					
Heterogeneity: Chi ² = 1	1.12, df = 3 (P =	0.77); l ² =	0%					
Test for overall effect: 2	Z = 0.34 (P = 0.7	'3)						
2.2.2 Minor complicat	tions							
Calliess et al.2017	0	100	0	100		Not estimable		
Dossett et al.2012	4	41	3	41	20.5%	1.37 [0.29, 6.54]		
Dossett et al.2014	3	60	3	60	21.5%	1.00 [0.19, 5.16]		
McEwen et al.2020	1	41	1	41	7.4%	1.00 [0.06, 16.55]		
Young et al.2017	3	49	3	50	21.1%	1.02 [0.20, 5.33]		
Subtotal (95% CI)		291		292	70.4%	1.11 [0.46, 2.70]		
Total events	11		10					
Heterogeneity: Chi ² = I			0%					
Test for overall effect: J	Z = 0.24 (P = 0.8)	11)						
Total (95% CI)		582		584	100.0%	1.16 [0.55, 2.41]	+	
Total events	15		13					
Heterogeneity: Chi ² =	1.25, df = 7 (P =	0.99); l² =	0%					- 4
Test for overall effect: 3	Z = 0.39 (P = 0.7	'0)					0.001 0.1 1 10	1
Test for subaroup diffe			1 (P = 0.88). I ² = 0%				Favours [Kinematic alignment] Favours [Mechanical alignment]	

Fig. 13 The forest plot for complication. Major complications are defined as revision of knee joint or removal of prosthesis caused by various reasons; and other additional surgery treatments were classified as minor complications.

KINEMATIC ALIGNMENT IN TOTAL KNEE ARTHROPLASTY

with KOA lacks long-term results, so it is necessary to collect detailed observations, perform studies with longer follow-up and data analysis, and scientifically evaluate the new treatment methods.

Limitations

However, some limitations still existed in this study. First, high heterogeneity existed in some comparisons. Although we used several subgroups, heterogeneity was still present in some results, and we failed to thoroughly explain the heterogeneity. Second, although the short-term clinical effect after KA-TKA has been evaluated, there is a lack of long-term follow-up results for the survival rate of the prosthesis. Finally, the chief limitation of this study was the small sample size; thus, a large sampler size, more rigorous RCTs, and

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longer follow-up supporting these results will be needed in the future.

Conclusion

This meta-analysis shows that the KA-TKA had better outcomes than the MA-TKA on WOMAC score, Combined KSS, KSS (Society and Function) score, and knee range of flexion at short-term follow-up.

Acknowledgments

We thank AJE for its linguistic assistance during the preparation of this manuscript.

Disclosure

The authors declare that we have no conflict of interest.

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