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KNEE ARTHROPLASTY

Outcome of kinematic alignment using patient-specific instrumentation versus mechanical alignment in TKA: a meta-analysis and subgroup analysis of randomised trials

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Abstract

Introduction Kinematic alignment (KA) in total knee arthroplasty (TKA) matches component position to the pre-arthritic anatomy of an individual patient, with the aim of improving functional outcomes. Recent randomised controlled trials (RCTs) comparing KA to traditional neutral mechanical alignment (MA) have been mixed. This collaborative study combined raw data from RCTs, aiming to compare functional outcomes between KA using patient-specific instrumentation (PSI) and MA, and whether any patient subgroups may benefit more from KA technique.

Materials and methods A literature search in PubMed, EMBASE and Cochrane databases identified four randomised controlled trials comparing patients undergoing TKA using PSI-KA and MA. Unpublished data including Western Ontario McMaster Universities Arthritis Index (WOMAC) and Knee Society Score (KSS) were obtained from study authors. Meta-analysis compared MA to KA change (post-op minus pre-op) scores. Subgroup-analysis on KA patients looked for subgroups more likely to benefit from KA and the impact of PSI accuracy.

Results Meta-analyses of change scores in 229 KA patients versus 229 MA patients were no different from WOMAC (mean difference 3.4; 95% confidence interval − 0.5 to 7.3), KSS function (1.3, − 3.9 to 6.4) or KSS combined (7.2, − 0.8 to 15.2). A small advantage was seen for KSS pain in the KA group (3.6, 95% CI 0.2–7.1). Subgroup-analysis showed no difference between varus, valgus and neutral pre-operative alignment groups, and those who did and did not achieve KA plans. Pain-free patients at 1-year were more likely to achieve KA plans.

Conclusion Patient-reported outcome scores following TKA using PSI-KA are similar to MA. No identifiable subgroups benefited more from KA, and long-term results remain unknown. Inaccuracy of the PSI system used in KA patients could potentially affect outcome.

Keywords Total knee arthroplasty · Kinematic alignment · Mechanical alignment · ShapeMatch · Patient-specific instrumentation

Introduction

The concept of mechanical alignment (MA) in total knee arthroplasty (TKA) is to position both the tibial and femoral components perpendicular to the mechanical axis of each

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bone, aligning the overall hip–knee–ankle (HKA) angle of the limb to neutral. This theory holds that MA optimises load distribution in TKA and will minimise implant failure though polyethylene wear or component loosening [1–5].

In contrast, kinematic alignment (KA) aims to position TKA implants to match the pre-arthritic anatomy of each individual patient. In the native knee, on average the articular surface of the tibia will be in slight varus and that of the femur in slight valgus. However, there is also significant variation, with over 30% of male non-arthritic patients reported to have a HKA angle of > 3° varus [6]. The KA technique aims to reproduce the individual patient anatomy and alignment, and KA advocates suggest this will improve soft tissue balancing, reduce the need for ligament releases, and enhance functional outcome following TKA [7–9].

Recently, several randomised controlled trials (RCTs) have been published comparing KA TKAs performed with patient-specific instrumentation (PSI, ShapeMatch, OtisMed Inc, Alameda, CA, USA) to standard MA technique, with conflicting results [7, 10–12]. This KA ShapeMatch technique is no longer commercially available, and this collaborative study between authors of these RCTs aims to combine data from the trials, to analyse functional and radiological outcomes of KA performed using PSI versus MA TKA. In addition, by combining raw data we hoped to identify whether subgroups of patients may be more likely to benefit from KA technique. Specifically, we sought to answer the following questions:

1. Using meta-analysis, do patient-reported outcome measures (PROMs) differ between patients treated with TKA using PSI kinematic alignment (KA) versus mechanical alignment (MA) techniques?
2. Are there differences in outcomes for KA for patient subgroups, such as whether the KA plan was achieved?
3. What are the differences between KA patients with good versus poor patient-reported outcome scores?

Materials and methods

A primary search was done using the electronic databases of PubMed (1950 to May 2016), EMBASE (1950 to May 2016) and Cochrane databases (1980 to May 2016), using the keywords: total knee replacement or arthroplasty AND kinematic* AND alignment*. A secondary search was done examining the reference list of relevant papers. Unpublished studies were searched using the meta-register of clinical trials [13]. The search strategy was in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14] (ESM Appendix 1). Eligibility criteria for study selection included RCTs comparing KA TKA technique versus MA in primary TKA using patient-specific instrumentation, reported functional and radiological outcomes, a follow-up period of at least 1 year with peer-reviewed published data.

Data were extracted and analysed and outcomes that were common across the studies were extracted independently onto a spreadsheet for statistical analyses (Table 1). This included: (1) patient demographics—sample size, sex, age, and body mass index (BMI), (2) PROMs—Knee Society Score (KSS, 0–100 worst to best), Western Ontario McMaster Universities Arthritis Index (WOMAC, converted to a scale of 0–100 worst to best) and the Oxford Knee Score (OKS, 0–48 worst to best), and (3) radiological outcomes—HKA angle, lateral distal femoral angle (LDFA), medial proximal tibial angle (MPTA) and tibial component slope (TCL). Data on post-surgical complications were recorded qualitatively. Unpublished data were obtained from the authors of three studies [10–12], including radiological data

Table 1 Overview of studies

Study	Calliess et al. [10]	Dossett et al. [7]	Waterson et al. [11]	Young et al. [12]
Sample size	88	200	71	99
Follow-up period	1 year	2 years	1 year	1 and 2 years
Surgical technique	Triathlon, fixed cemented, CR	Vanguard, fixed cemented, CR	Triathlon, fixed cemented, CR	Triathlon, fixed cemented, CR
PROMs of interest (published and unpublished)	KSS pain and function, WOMAC	KSS pain and function, WOMAC, OKS	KOOS, KSS function	KSS pain and function, WOMAC, OKS
Radiology	HKA, LDFA, MPTA, tibial slope	HKA, LDFA, MPTA	HKA, LDFA, MPTA	HKA, LDFA, MPTA, tibial slope
Quality assessment				
EPHPP	3	2	1	1
CCRBT	High risk	Low risk	Low risk	Low risk
Jadad	1	5	4	5

EPHPP Effective Public Health Practice Project, *CCBRT* Cochrane Collaboration's tool for assessing risk of bias in randomised trials on individual study patients and unpublished outcomes such as WOMAC (derived from Knee and Osteoarthritis Outcome Score, KOOS [11]) and KSS pain and function components [10]. Despite attempts, authors of a fourth study did not respond to requests for additional data, therefore only published results were included in the analysis [7, 8].

Methodological quality and risk of bias was assessed using three different modalities to incorporate different measured constructs and improve reliability [15, 16] (ESM Appendix 2): (1) the Quality Assessment Tool for Quantitative Studies (Effective Public Health Practice Project, EPHPP, McMaster University, Ontario, Canada), (2) the Cochrane Collaboration's tool for assessing risk of bias in randomised trials (CCRBT) [17], and (3) the Jadad scale [18]. Two reviewers conducted the appraisal for each study independently and any discrepancy was resolved by consensus.

Statistical analysis

Meta-analyses were conducted on pre-operative and post-operative change scores for WOMAC and KSS (pain, function and combined) between KA and MA groups. The change scores were pooled using the standardised mean differences, accounting for heteroscedastic variances for each population between the two groups [19, 20]. P values < 0.05 were considered significant. Post-surgical radiological outcomes were also compared between KA and MA groups.

Subgroup analyses were conducted on three parameters in the KA group: (1) pre-operative alignment subdivided into varus, valgus and neutral (defined as a pre-operative HKA angle $< -3°$, $> 3°$ or between -3 and 3, respectively), (2) if post-operative alignment (HKA, LDFA, and MPTA) was within 3° of the ShapeMatch plan, and (3) patients who were relatively 'pain-free' at 1-year post-operation (defined as a WOMAC ≥ 80). For (2), covariate analysis was done on WOMAC and KSS 1-year post-operative scores, accounting for pre-operative scores, pre-operative alignment and study centres. For (3), multiple logistics regression was used to analyse the data.

Results

Literature search

Four studies were selected for analysis in this review (Fig. 1). The primary and secondary searches resulted in 373 records. Examination of title/abstract excluded 355 records, and a further 14 were excluded after the studies were examined closely. Eight studies on kinematic alignment lacked a comparative group [21–28]. One was excluded as it was a retrospective cohort analysis that did not examine functional scores [29]. Two studies were excluded based on an inappropriate patient cohort: one consisted of revision TKAs following unicompartmental knee arthroplasty [30] and another was a repeat cohort of a selected study [8]. One was an incomplete study [31] and one used a different method to establish KA [32]. The meta-register of clinical trials yielded three studies that would meet the criteria for inclusion, but all were either abandoned or incomplete.

Study characteristics and quality

Two authors conducted quality assessment on the four studies using three different methods (Table 1, ESM Appendix 2). Two of four studies scored a strong rating while the other two scored a moderate and weak rating. When combining outcomes for analysis, two studies used full WOMAC version [7, 10], one used a reduced version [12] and the other derived the reduced version from the KOOS score [11]. Comparisons of full and reduced WOMAC scales are highly valid (correlation coefficient of 0.96) [33]. Three of the four studies had follow-up data at 1 year [10–12], and two had follow-up data at 2 years [8, 12]. Recent studies showed that post-operative function scores are largely predictive of long-term scores [34, 35]. The KSS pain component for one study was derived from a VAS scale [11]. The standard deviation (of change scores) from one study was not included as this was not available in published data [7].

Pooled outcomes

The pooled mean difference in change scores (post-minus pre-operative scores) between KA and MA were 3.4 [95% confidence interval (CI) − 0.5, 7.3; Fig. 2a], 3.6 (0.2, 7.1; Fig. 2b), 1.3 (− 3.9, 6.4; Fig. 2c) and 7.2 (− 0.8, 15.2; Fig. 2d) for WOMAC, KSS pain, function and combined, respectively. There were no significant differences in function scores between KA and MA groups as zero was included in the 95% CI. The 95% CI for WOMAC and combined KSS had a lower boundary close to zero and an upper boundary far from zero, suggesting a trend to a higher score in the KA group. Mean difference in KSS pain was 3.6 points higher in the KA than the MA group (95% CI 0.18–7.1). There was no significant heterogeneity in treatment effect in all four studies regarding KSS (pain, function and combined) and WOMAC scores (p values were between 0.18 and 0.41, Fig. 2).

The pooled mean difference in post-surgical radiological angles were 0.4 (95% CI − 0.9, 1.7), 1.4 (0.9, 1.9) and − 1.7 (− 2.4, 1.0) for HKA, LDFA and MPTA angles, respectively (Table 2). Heterogeneity exists between radiological outcomes ($p = < 0.01$, Table 2).

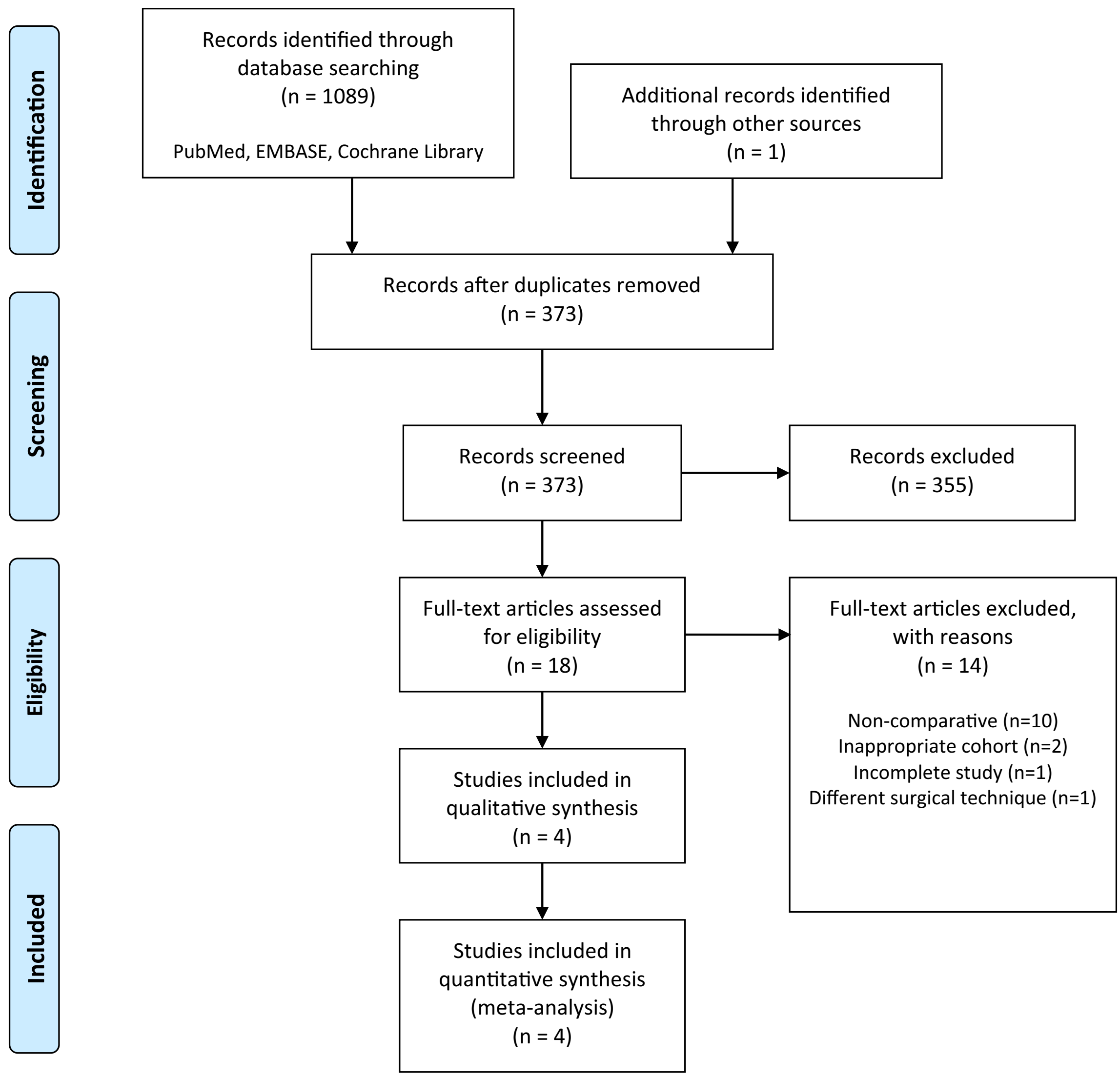


Fig. 1 PRISMA search strategy

Subgroup-analysis

Pre-operative alignment

Analysis of variance indicates that in the pooled data of three studies [10–12], there were no significant differences in 1 year change scores of KSS combined and WOMAC across the three pre-operative alignment groups of varus, neutral, or valgus (Table 3).

ShapeMatch (SM) plan achieved

Almost 25% of the patients were more than 3° outside the pre-operative KA plan with respect to HKA. Planes other than the coronal plane could not be evaluated, because they were not available from the KA planning algorithm. However, there was no significant difference in function scores (WOMAC and KSS function) between those that achieved their SM plans (within 3°) and those that did not (Table 4). There was no significant difference in KSS pain between those that achieved HKA and LDFA SM plans versus those that did not, but KSS pain was different between those that achieved MPTA SM plans and those that did not ($p = 0.01$).

Characteristics of 'pain-free' group (WOMAC score ≥ 80)

Multiple logistic regression analysis showed that patients are more likely to be pain-free at 1 year if the absolute difference between SM planned and post-operative measured MPTA was lower ($p < 0.001$, Table 5) when controlling for other confounders (pre-operative WOMAC and pre-operative

a. WOMAC	KA			MA				
Study	Mean	SD	Total	Mean	SD	Total	Weight %	Mean difference [95% CI]
Calliess et al., 2016	50**	29**	100	45**	15**	100	64.9	4.90 [-1.55, 11.35]
Dossett et al., 2016	40**		44	33**		44	7.5	6.30 [-3.99, 16.59]
Waterson et al., 2016	29***	15***	36	31***	21***	35	19.9	-3.90 [-12.86, 5.06]
Young et al., 2017	38	18	49	35	19	50	7.7	4.80 [-2.44, 12.04]
Results from meta-analysis			**229**			**229**	**100**	**3.39 [-0.53, 7.31]**

Heterogeneity: Tau^2 = 0; Q (df = 3) = 3.2 (p = 0.36); I^2 = 0%

b. KSS pain	KA			MA				
Study	Mean	SD	Total	Mean	SD	Total	Weight %	Mean difference [95% CI]
Calliess et al., 2016	39	19	100	36	15	100	64.9	2.90 [-1.88, 7.68]
Dossett et al., 2016	38		44	27		44	7.5	11.00 [1.54, 20.46]
Waterson et al., 2016	41*	17*	36	41*	18*	35	19.9	0.70 [-7.63, 9.03]
Young et al., 2017	54	19	49	50	17	50	7.7	3.10 [-5.21, 11.41]
Results from meta-analysis			**229**			**229**	**100**	**3.64 [0.18, 7.09]**

Heterogeneity: Tau^2 = 0; Q (df = 3) = 2.9 (p = 0.41); I^2 = 0%

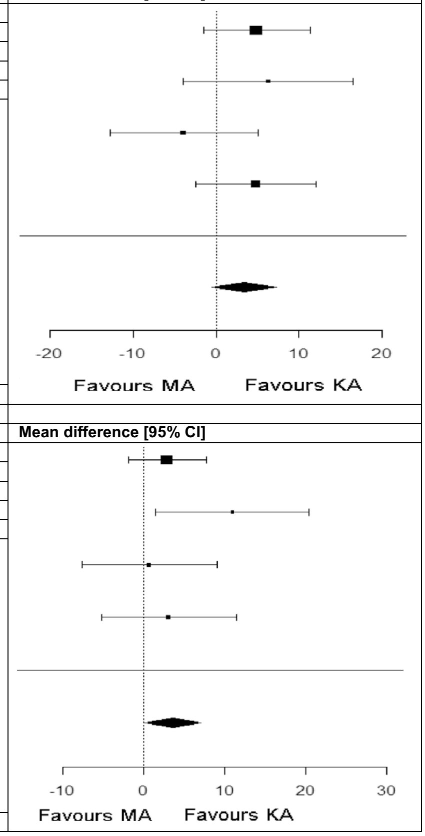


Fig. 2 Forest plot of the difference between post-operative and pre-operative scores in KA and MA patients across four RCTs: **a** WOMAC, **b** KSS pain, **c** KSS function, **d** KSS combined. *KA* kinematic alignment, *MA* mechanical alignment. Asterisk: KSS Pain derived from VAS. Double asterisk: WOMAC conversion to 0–100 (worst to best). Triple asterisk: WOMAC derived from KOOS

alignment groups). Analysis was not done on age and sex as data were not available for one study [10]. There were no significant differences with pre-operative alignment (varus, valgus and neutral). HKA and MPTA angles were positively correlated (Pearson's correlation coefficient 0.4, $p < 0.001$).

Discussion

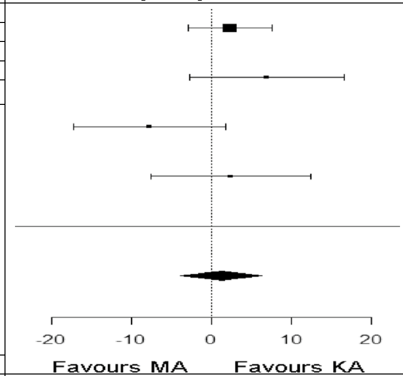
A significant percentage of patients report dissatisfaction with the outcome of TKA performed using traditional MA technique [36, 37]. Advocates of KA technique argue that more closely reproducing individual patient anatomy and kinematics will enhance the functional outcome of TKA, and potentially prevent unexplained pain [38]. Others point out the original rationale for MA technique was to enhance implant durability, and argue the alterations in alignment of KA may compromise survivorship [39]. While currently the long-term results of kinematically aligned TKA are unknown, this meta-analysis found that early patient-reported outcome measures with KA performed with PSI are similar to those of MA.

There are several limitations to this study. Firstly, all included RCTs used PSI manufactured by a single company (OtisMed Inc, Alameda, CA, USA) for the KA group and used proprietary software analysis of the pre-operative MRI scan to determine the target 'kinematic' alignment, therefore these results may not be generalizable to other "KA" techniques, such as those using manual instrumentation [23, 40]. However, the consistent technique across the four randomised trials is also a strength of the meta-analysis, as there may be significant variations in technique between surgeons using alternative 'kinematic' alignment methods [9, 21, 26, 41]. Furthermore, as these guides are no longer commercially available, no further RCTs using this method of KA are expected, and this study represents an important opportunity to examine combined data. Secondly, the follow-up period in all four studies (< 2 years) was too short to assess long-term complications, such as component loosening, and the long-term effect of KA remains unknown [42, 43]. Finally, while we obtained raw data from three studies, we

c. KSS function	KA			MA				
Study	Mean	SD	Total	Mean	SD	Total	Weight %	Mean difference [95% CI]
Calliess et al., 2016	34	22	100	32	16	100	64.9	2.40 [-2.86, 7.66]
Dossett et al., 2016	26		44	19		44	7.5	7.00 [-2.75, 16.75]
Waterson et al., 2016	28	25	36	36	15	35	19.9	-7.70 [-17.28, 1.88]
Young et al., 2017	30	21	49	23	24	50	7.7	2.50 [-7.55, 12.55]
Results from meta-analysis			**229**			**229**	**100**	**1.27 [-3.86, 6.41]**

Heterogeneity: Tau^2 = 9.7; Q (df = 3) = 4.9 (p = 0.18); I^2 = 34.9%

Mean difference [95% CI]



d. KSS combined	KA			MA				
Study	Mean	SD	Total	Mean	SD	Total	Weight %	Mean difference [95% CI]
Calliess et al., 2016	73	36	100	68	27	100	64.9	5.30 [-3.47, 14.07]
Dossett et al., 2016	63		44	46		44	7.5	17.00 [1.15, 32.85]
Waterson et al., 2016	70	33	36	74	27	35	19.9	-4.00 [-17.87, 9.87]
Young et al., 2017	77	34	49	74	34	50	7.7	13.90 [-0.67, 28.47]
Results from meta-analysis			**229**			**229**	**100**	**7.20 [-0.83, 15.24]**

Heterogeneity: Tau^2 = 24.5; Q (df = 3) = 4.9 (p = 0.18); I^2 = 36.3%

Mean difference [95% CI]

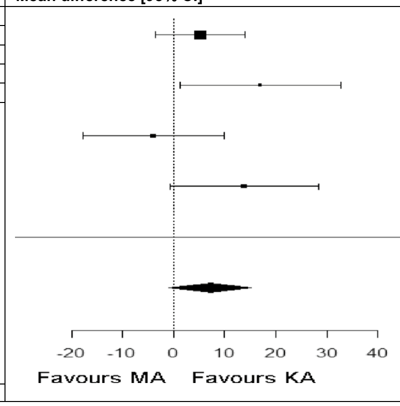


Fig. 2 (continued)

were unable to obtain data from authors of the fourth study. Fortunately the clinical and radiographic findings of this study were published in detail across two manuscripts [7, 8], and these results were included in our main meta-analysis.

Four previous systematic reviews have attempted to combine published data comparing KA versus MA, generally reporting functional results in favour of KA [44–47]. Lee et al. performed a descriptive review, including only three published RCTs and a number of non-comparative case series from a development centre for KA PSI guides [45]. Courtney et al. combined data from the same four RCTs as our study in a meta-analysis, reporting findings favourable to KA [44]. However, as the published RCT manuscripts do not include all details of the WOMAC or KSS scores, Courtney et al. were able to look at a single PROM only: the total KSS score [44]. They also lacked pre-operative PROMs, whereas by sharing raw data we were able to analyse change scores (post-minus pre-operative scores) for multiple PROMS. Pre-operative scores are strongly related to post-operative scores in an individual patient, and inter-study differences in absolute pre-operative scores between MA and KA groups tended to favour KA. In a more recent review, Li et al. combined data from six studies in a meta-analysis, concluding KA resulted in better functional outcomes than MA [46]. They reached six studies by including a non-randomised study of 22 patients undergoing revision TKA from a failed UKA. They also included data on the patients from Dossett el al twice, including the separately published scores at 6 and 24 months [7, 8]. Given the Dossett study findings were strongly favourable to KA, including these patients twice calls into question the validity of the meta-analysis. Yoon et al. also included six studies in their meta-analysis, again including Dossett et al's study twice [47]. They also included 144 patients from an abstract describing a potential KA versus MA study [31]. The abstract reported early (6 months) outcomes on the first 17 patients (6 KA and 11 MA). The study was never completed, however Yoon et al. extrapolated these initial findings to apply to all 144 potential patients, essentially including 127 patients in their meta-analysis that do not exist.

In contrast to these previous reviews, we found no statistical difference in improvement between KA and MA for WOMAC, KSS combined or KSS function scores, and only a small advantage to KA in KSS pain scores. The methodological differences above may explain these findings, and any advantage to KA over MA in these previous reviews is likely to have been overstated [44, 45].

Table 2 Summary of radiological outcomes

Study	Calliess et al. [10]		Dossett et al. [7]		Waterson et al. [11]		Young et al. [12]		Pooled mean difference (95% CI)	Heterogeneity Q testing (p value)
Treatment group	KA	MA	KA	MA	KA	MA	KA	MA		
n	100	100	44	44	36	35	49	50	229	
HKA (SD)	1 (3)	− 1 (1)	− 0.1 (2.8)	0.1 (2.5)	− 0.7 (4.4)	− 0.5 (3.9)	− 0.4 (3.5)	− 0.7 (2.0)	0.39 (− 0.94, 1.71)	83.1% (0.00)
LDFA (SD)	2 (2)	1 (0)	1.3 (2)	− 0.8 (2.7)	1.4 (2.2)	0.1 (2.4)	2.1 (2.5)	0.5 (1.6)	1.38 (0.88, 1.89)	91.0% (<0.00)
MPTA (SD)	− 2 (1)	− 1 (0)	− 2.2 (2.6)	0 (2.1)	− 3.1 (2.8)	− 0.9 (2.0)	− 2.6 (3.1)	− 0.7 (1.8)	− 1.68 (− 2.38, − 0.99)	68.3% (<0.00)
Tibial slope (SD)	5 (3)	5 (3)	5 (5.4)*	3 (4.7)*	NA	NA	4 (2.5)	1.3 (2)	0.84 (0.67,1.01)	80.7% (0.00)

Positive values are in valgus (converted for Calliess and Dossett)

Waterson values obtained from raw data

HKA hip–knee–ankle, *LDFA* lateral distal femoral angle, *MPTA* medial proximal tibial angle, *KA* kinematic alignment, *MA* mechanical alignment

[a]From Dossett et al. [8]

Table 3 Subgroup analysis of pre-operative alignment in the kinematic group from three studies

Study	Alignment	Sample size	WOMAC (SD)			p	KSS pain (SD)			KSS function (SD)			KSS combined (SD)			p
			Pre	1y	Δ		Pre	1y	Δ	Pre	1y	Δ	Pre	1y	Δ	
Calliess et al. [10]	Varus	45	39 (22)	88 (18)	45 (35)		50 (11)	95 (6)	45 (14)	60 (12)	96 (11)	36 (15)	110 (16)	190 (12)	81 (20)	
	Valgus	10	41 (19)	97 (5)	56 (18)		59 (8)	91 (9)	32 (8)	56 (14)	99 (3)	43 (14)	115 (19)	189 (8)	74 (16)	
	Neutral	44	36 (18)	91 (14)	55 (21)		56 (13)	94 (11)	38 (14)	60 (12)	95 (10)	36 (18)	115 (21)	190 (14)	74 (26)	
Waterson et al. [11]	Varus	21	57 (12)	89 (12)	32 (13)		48 (13)	93 (8)	41 (20)	55 (20)	90 (14)	29 (34)	99 (3)	169 (51)	70 (48)	
	Valgus	3	52 (8)	65 (24)	13 (19)		52 (15)	81 (8)	29 (20)	37 (28)	70 (44)	33 (16)	89 (39)	151 (48)	62 (17)	
	Neutral	3	71 (19)	96 (1)	25 (20)		61 (18)	91 (13)	30 (32)	80 (14)	78 (32)	− 3 (18)	141 (4)	168 (45)	27 (50)	
Young et al. [12]	Varus	40	52 (13)	91 (11)	37 (22)		34 (15)	78 (13)	45 (23)	53 (16)	84 (18)	30 (27)	87 (26)	156 (38)	74 (42)	
	Valgus	7	41 (13)	83 (31)	42 (31)		50 (14)	86 (14)	37 (21)	61 (12)	90 (15)	29 (16)	110 (20)	176 (29)	66 (34)	
	Neutral	3	85 (14)	93 (9)	45 (11)		48 (4)	70 (19)	23 (15)	57 (12)	70 (10)	13 (6)	104 (14)	140 (27)	36 (19)	
Combined data	Varus	106	46 (19)	89 (15)	40 (28)		43 (15)	89 (12)	44 (18)	56 (15)	90 (15)	32 (24)	99 (25)	175 (35)	77 (34)	
	Valgus	20	43 (16)	87 (23)	45 (27)	0.27	55 (12)	88 (11)	33 (15)	55 (17)	91 (20)	37 (16)	110 (23)	179 (27)	69 (23)	0.43
	Neutral	50	38 (19)	90 (14)	53 (22)	0.87	55 (13)	92 (12)	37 (15)	60 (13)	93 (13)	33 (20)	116 (21)	185 (20)	70 (29)	0.41

p value: analysis of variance showed no difference in WOMAC or KSS combined scores between varus, valgus or neutral pre-operative alignment groups in the combined data

Table 4 Subgroup analysis of patients that achieved HKA ShapeMatch plans in the kinematic group

Angle	SM plan achieved	Sample size	WOMAC—mean (SD)				KSS pain—mean (SD)				KSS function—mean (SD)				KSS combined—mean (SD)			
			Pre	1y	Δ	p	Pre	1y	Δ	p	Pre	1y	Δ	p	Pre	1y	Δ	p
HKA	Yes	126	45 (19)	90 (16)	44 (23)		48 (14)	89 (12)	41 (16)		58 (15)	91 (15)	33 (19)		105 (24)	180 (22)	75 (27)	
	No	40	37 (19)	88 (16)	51 (23)	0.54	52 (14)	92 (11)	39 (16)	0.43	56 (15)	93 (13)	37 (19)	0.58	108 (25)	185 (20)	75 (28)	0.78
LDFA	Yes	148	43 (19)	89 (16)	47 (24)		49 (15)	90 (12)	41 (17)		57 (15)	91 (16)	35 (20)		105 (25)	181 (23)	76 (29)	
	No	18	48 (17)	88 (16)	40 (20)	0.17	49 (14)	89 (12)	40 (17)	0.73	63 (11)	94 (8)	31 (13)	0.07	113 (20)	183 (17)	70 (22)	0.29
MPTA	Yes	151	43 (19)	89 (16)	46 (24)		48 (15)	90 (13)	42 (17)		57 (15)	91 (15)	34 (19)		105 (25)	181 (23)	76 (28)	
	No	15	42 (22)	89 (18)	48 (24)	0.75	60 (6)	90 (10)	30 (11)	0.01	59 (16)	91 (16)	33 (23)	0.82	118 (20)	181 (20)	64 (25)	0.12

A further advantage of sharing raw data in this study, was the ability to perform more detailed subgroup analysis, to identify whether KA may be of more benefit in certain patients. Bone morphotypes of the varus and valgus knee are known to differ, and any advantage to KA may depend on the pre-operartive alignment profile [48]. With the numbers available, we were unable to identify pre-operative alignment parameters which might be more suitable to KA technique. This is important as each trial included in this study differed slightly in their inclusion criteria regarding alignment parameters, with variable boundaries/inclusion criteria as to what was acceptable deformity. This reflects the fact that several questions regarding KA technique remain unanswered, such as whether patients with higher degrees (e.g. > 3°) of pre-operative varus should be placed in their natural 'kinematic' alignment or corrected closer to neutral. There is evidence that excessive varus increases load at the implant-bone interface and may compromise survivorship [42, 49], however clinical data is mixed [43] and reported mid-term results of KA are encouraging [22]. Factors such as the degree of post-operative component varus or valgus alignment [49], and patient age and BMI [50] are likely to be important, but currently there is conflicting data with which to define 'acceptable' alignment parameters, and how these will affect the functional outcome of KA technique.

We also performed subgroup analysis to assess whether accuracy of the PSI guides affected KA outcome. We were only able to evaluate the coronal alignment, because rotational and sagittal planes were not outputted in the KA planning algorithm. While the accuracy of this PSI system was validated in a clinical study [51], we found a significant number of patients did not meet their initial KA plan. Our findings on whether this affected clinical outcome was mixed. We did not find a difference in outcome between patients who 'achieved' versus 'did not achieve' their coronal alignment parameters. However, in patients with a 'good' WOMAC score a higher percentage were within 3° of their planned MPTA angle than in those with a poor WOMAC score. This raises the question whether surgical techniques that achieve higher precision (e.g. robotics) may be able produce a more positive outcome using KA principles.

In conclusion, this analysis of level 1 studies found pain and functional improvements were equivalent between KA using PSI and MA techniques in primary TKA. Pooled data for function scores showed a trend towards a greater benefit in the KA group, but any advantage as measured by these instruments appeared small. Subgroup-analysis suggests that differences in pre-operative alignment did not alter outcomes with the KA technique, and we found mixed evidence that the inaccuracy of the PSI technique may play a role regarding the clinical outcome of KA. Future research should focus on safe alignment boundaries and whether the alterations in alignment using KA technique alter long term durability.

Table 5 Subgroup analysis of patients that were 'pain-free' at 1 year in the kinematic group

First author	Young		Waterson		Calliess		Combined	
1y WOMAC ≥ 80	No	Yes	No	Yes	No	Yes	No	Yes
Sample size (n)	8	40	5	12	13	85	26	137
Age (SD)	64 (9)	70 (6)	74 (8)	78 (7)	NA	NA	68 (10)	72 (7)
Sex (% M)	50	58	50	67	NA	NA	50	61
Pre-op WOMAC	49 (14)	50 (13)	50 (7)	60 (12)	36 (22)	37 (19)	43 (19)	44 (18)
Varus (%)	75	83	60	75	54	42	62	58
Valgus (%)	13	13	40	8	8	12	15	12
Neutral (%)	13	5	0	16	38	46	23	31
Pre-operative HKA (SD)	− 6 (6)	− 6 (6)	0 (10)	− 7 (6)	− 3 (5)	− 3 (5)	− 4 (7)	− 4 (6)
ShapeMatch plan HKA (SD)	0 (3)	0 (3)	0 (4)	− 2 (3)	− 1 (2)	1 (2)	− 1 (3)	− 1 (2)
ShapeMatch plan MPTA (SD)	− 1 (3)	− 2 (2)	− 1 (2)	− 4 (2)	− 3 (1)	− 3 (1)	− 3 (2)	− 3 (2)
Post-operative HKA (SD)	− 3 (2)	0 (3)	1 (8)	− 1 (3)	2 (4)	1 (3)	− 1 (5)	0 (3)
Post-operative MPTA (SD)	− 1 (4)	− 3 (3)	− 4 (4)	− 3 (3)	− 2 (2)	− 1 (2)	− 1 (4)	− 2 (3)

Multiple logistic regression analysis: the difference between SM planned and post-operative measured MPTA was significantly lower in the pain-free group ($p < 0.001$) when controlling for other confounders (pre-operative WOMAC and pre-operative alignment groups). There were no significant differences with pre-operative alignment (varus, valgus and neutral). HKA and MPTA angles were positively correlated (Pearson's correlation coefficient 0.4, $p < 0.001$)

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