



CLINICAL ARTICLE

Computer Navigation Assisted Restricted Kinematic Alignment Improves Short-Term Outcomes in Total Knee Arthroplasty: An Ambispective Cohort Study

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Objectives: Mechanical alignment (MA)-total knee arthroplasty (TKA) has been challenged due to the excessive soft tissue release and the evidence of the clinical outcomes of computer assisted navigation is still limited. The aim of this ambispective cohort study was to: (i) investigate whether computer assisted navigation is capable to achieve restricted kinematic alignment (rKA)-TKA; and (ii) compare the short-term outcomes between rKA-TKA and MA-TKA.

Methods: We retrospectively included 41 patients diagnosed with osteoarthritis who received MA-TKA between April 2019 and January 2021 and 43 patients diagnosed with osteoarthritis who received rKA-TKA were included in the prospective cohort from January 2021 to September 2021. Demographical, peri-operative, and radiological data were collected and compared. Unpaired two-sample *t*-test for continuous variables and χ^2 test for categorical variables were used to compare various measurements in two groups. The patient-reported outcome measures at baseline, 10 days (T1), and 6 months (T6) after surgery were statistically analyzed by generalized estimating equation (GEE) models.

Results: Forty-one patients (45 knees) and 43 patients (48 knees) were included in the MA and the rKA group respectively. Three constitutional knee phenotypes (II, I, IV) were the commonest in our population. Navigation improved the surgical accuracy (1.5° vs 3.5°, $p < 0.001$) and precision (interquartile range 4.0 vs 2.0, $p < 0.001$) in the rKA group than the MA group. The changes in Knee Injury and Osteoarthritis Outcome Score 12 (KOOS12), EuroQol five-dimension questionnaire (EQ5D) from baseline to T1 and T6 for patients with on-target rKA were larger than on-target MA counterparts (26.053 vs 18.607, $P < 0.001_{(KOOS12, T1)}$, 0.457 vs 0.367 $p < 0.001_{(EQ5D, T1)}$; 51.017 vs 46.896, $P = 0.023_{(KOOS12, T6)}$, 0.606 vs 0.565, $P = 0.01_{(EQ5D, T6)}$). Patients with on-target rKA had better Forgotten Joint Score (FJS) at T1 (54.126 vs 40.965, $P = 0.002$) compared with on-target MA counterparts.

Conclusions: Computer assisted navigation achieved the level of accuracy required by rKA-TKA. rKA-TKA offered significantly better short-term outcomes than MA-TKA.

Key words: Alignment; Navigation; Patient report outcome measures; Total knee arthroplasty

Introduction

As the global population ages, more and more people are suffering from osteoarthritis and it was estimated the aging of the population would result in about 1.9 million

individuals with total knee arthroplasty (TKA) by 2030.¹ However, it has been reported that up to 20% of patients are not satisfied with their new joints, and this may be due to significant kinematic changes.²⁻⁴ Thus, conventional

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mechanical alignment (MA) which pursues the completely neutral alignment of the knee has been challenged due to its standardized procedure without consideration of individual anatomy and excessive soft tissue release.⁵ To solve this dilemma, kinematic alignment (KA) was developed to restore constitutional limb anatomy. The philosophy of KA is to make the implant thickness equal to the exact amount of removed bone or cartilage to restore the diverse pre-arthritis knee joint orientation in the population.⁶ The KA is thought to be available in primary osteoarthritis without severe deformity.⁷ However, the safe range for kinematically positioned total knee components remains to be determined.⁸ Besides, an osteoarthritic knee may be different from its pre-arthritis status. Therefore, the restricted kinematic alignment (rKA) is developed as a compromise for MA and KA.⁹ It brings back the extreme anatomies toward acceptable ranges and it has been highlighted in publications that rKA introduces significantly less change to normal anatomy compared with MA, and thereafter has a favorable effect on normal biomechanics, leading to a more balanced flexion and extension places in medial and lateral compartments.^{10,11} A limited amount of publications demonstrated that rKA is associated with better patient-reported outcome measures (PROMs),^{12,13} and the short-term PROMs of rKA-TKA remain to be investigated.

The traditional manual method cannot fulfill the requirement of rKA-TKA implementation as it requires higher accuracy for individualized alignment. The development of new techniques including patient specific instrumentation (PSI), navigation, and robotic surgery improved the surgical precision of TKA,¹⁴ which may be applicable in rKA-TKA. However, errors still existed in executing surgical plans with the use of new techniques.^{15,16} Therefore, when implementing rKA-TKA with new techniques such as navigation, it is crucial to assess and consider the errors in intraoperative execution. Additionally, the combination of individualized rKA planning and navigation assisted execution remains poorly investigated. The evidence of whether this approach would improve the clinical outcome is limited.

The aim of this clinical observation-driven ambispective cohort study was to: (i) investigate whether computer assisted navigation is capable to achieve rKA-TKA; and (ii) compare the short-term PROMs between patients who receive rKA-TKA and patients who were treated MA-TKA. We hypothesize that computer assisted navigation is a reliable and effective approach to performing rKA-TKA, and rKA-TKA offered significantly better short-term outcomes than MA-TKA.

Methods

Study Design and Participants

An ambispective cohort study was conducted after being approved by the Institutional Review Board (IRB No. JS-2775). Retrospectively, between April 2019 and January 2021, consecutive patients listed at our clinic who exclusively underwent primary mechanical aligned TKA (MA-TKA) were screened. Cases were considered eligible for inclusion if:

(i) were diagnosed with osteoarthritis; (ii) were scheduled for cruciate-retained (CR), primary, unilateral or bilateral TKA; (iii) were between 18 and 80 years old; and (iv) were capable of accomplishing minimum 6 months follow-up. Patients were excluded if they: (i) had a severe joint deformity (varus or valgus over 20°) or unstable knee; (ii) had peripheral nervous system disease, rheumatological diseases, or dementia; and (iii) had a history of open knee surgery. Forty-one patients with 45 knees who underwent MA were included. In the prospective cohort, 43 patients with 48 knees were consecutively included with the same inclusion and exclusion criteria from January 2021 to September 2021. These patients received restricted kinematic aligned TKA (rKA-TKA). All procedures of MA and rKA group were performed by one experienced arthroplasty surgeon and his team at a single institution. Perioperative management and standardized physical therapy were conducted by the same team.

Coronal Plane Alignment of Knee Classification

The full-length weight-bearing phase of lower limbs was obtained from all patients. The hip-knee-ankle (HKA) angle, lateral distal femoral angle (LDFA), and medial proximal tibial angle (MPTA) of each participant were measured by two experienced researchers separately. According to the coronal plane alignment of knee (CPAK) classification introduced by MacDessi *et al.*¹⁷ we identified “the arithmetic HKA” (aHKA) using the algorithm: $aHKA = LDFA - MPTA$. A positive aHKA indicates varus and a negative aHKA indicates valgus constitutional alignment. We also determined joint line obliquity (JLO) using the algorithm: $JLO = LDFA + MPTA$. Combining aHKA and JLO, patients were divided into nine groups. Boundaries were determined according to the standard deviation of aHKA ($SD = 6$) and JLO ($SD = 3$) of our samples.

Preoperative Plans and Surgical Procedure

Surgical planning was scheduled based on HKA, LDFA, and MPTA. All patients received a cruciate-retaining total knee prosthesis (Legion; Smith & Nephew, Memphis, TN, USA), and a tourniquet was applied during the operation. In the MA group, HKA was set to a neutral (0°) alignment. The femoral component was set to 3° externally rotated to the posterior condylar axis. In the rKA group, surgery was planned following the “restricted KA protocol” introduced by Vendittoli *et al.*¹¹ The goal is to restore the constitutional alignment of the knee within a safe zone. In the coronal plane, the safe zone of both MPTA/LDFA was within $\pm 5^\circ$ of neutral while the safe zone of HKA was within $\pm 3^\circ$. If the preoperative planned LDFA/MPTA resections would lead to an HKA outside the safe zone of $\pm 3^\circ$ of neutral, then LDFA and/or MPTA were adjusted to restrict HKA within the boundaries of the safe zone. A computer assisted navigation system was applied to conduct rKA TKA (Brainlab Knee3; Smith & Nephew, Memphis, TN, USA). Specifically, after incision and exposure to the knee joint, the tibial and femoral array was placed and visibility was checked. Anatomical landmarks of the femur and tibia

were registered. The leg was brought to full extension/flexion with varus/valgus stress to test stability, and based on the stability information at this stage, an intraoperative plan of target alignment was derived. The navigation plane tool was attached to the cutting block, and bone resection was performed. The femur was first resected, followed by the tibia resection. The resected surface was verified to judge if the deviation from the desired position could be accepted or needed a reassessment of the cut. After performing the resection and verification, the spacer block was placed to assess leg alignment, stability, and medial/lateral gaps during rotation. Trial components were inserted to perform final verification, followed by prosthesis placement (Fig. 1).

Data Collection and Postoperative Outcomes

Demographical information, hemoglobin, and hematocrit before surgery, 1 and 3 days after surgery were collected from the hospital information system. A radiological assessment of postoperative alignment was undertaken 3 days after surgery. The results of coronal plane HKA, LDFA, and MPTA were averaged after two different experienced researchers independently measured the same image, and the Pearson correlation coefficients were used to measure the consistency of inter-observer comparisons. The primary endpoint of the cohort study was the completion of a 6-month postoperative follow-up. Patient-reported outcome measures (PROMs) at baseline (T0) and time point of 10 days (T1) and 6 months (T6) after the operation was recorded by one trained fellow. The PROMs included: (i) the Knee Injury and Osteoarthritis Outcome Score 12 (KOOS12), the aggregated mean score of subscales: pain, function (activities of daily living and sport/recreation), and quality of life; (ii) the EuroQol five-dimension questionnaire (EQ5D), representing overall health status. The relevant coefficients and norms of EQ5D for the Chinese population were applied to the model;¹⁸ and (iii) Forgotten Joint Score (FJS), indicating patients' awareness of their replaced knees in daily life. The validity and reliability of all three PROMs have been thoroughly studied,¹⁹ and all three PROMs have been shown to meet the requirements for psychometric validation and can be recommended to use as measures of TKA outcome.

Statistical Analysis

Summary statistics for demographic characteristics and clinical measures for subjects in the MA group and the rKA group were presented as mean (standard deviation, 95% confidence interval [CI]) for continuous variables and frequency (percentage) for categorical variables. Two-sample tests (unpaired two-sample *t*-test for continuous variables and χ^2 test for categorical variables) were used to compare various measurements in two groups.

To incorporate the repeated measure study design, we used the generalized estimating equations (GEE) approach to assess the effect of alignment on the post-operation measure for each of the PROMs (change in KOOS12 from baseline, change in EQ5D from baseline, and FJS) while adjusting for

demographic characteristics and clinical measures that might have influenced the outcome of interest. All the covariates were standardized before the model was fitted. It was also assumed that there was statistical significance when $P < 0.05$. Analyses were performed in SAS 9.4 (SAS Institute, Cary, NC, USA) and GraphPad Prism 9.0 (GraphPad Software, San Diego, CA, USA).

Given the sample size ($n_{MA} = 45$, $n_{rKA} = 48$) in this study, it was possible to detect an effect size (minimal detectable difference in units of standard deviation) of 0.6 for 80% statistical power at the significance level of 0.05.

Results

Demographic

For the mechanical alignment (MA) group, a total of 41 (45 knees) patients met the inclusion criteria, and a total of 43 (48 knees) patients were included in the restricted kinematic alignment (rKA) group. Among these patients, there were 32 (78.0%) females and 37 (86.0%) females in the MA group and the rKA group, respectively. The mean age of the MA group and the rKA group was 67.4 (95% CI 65.5–69.4) years and 69.3 (95% CI 67.3–71.2) years respectively. The BMI (in kg/m^2) of the rKA group (mean = 27.2, 95% CI 26.2–28.2) is larger than the MA group (mean = 25.2, 95% CI 24.3–26.2) with a significant difference ($P = 0.005$). We measured the preoperative lower limb alignments (in degrees) of both groups of patients. There was no significant difference in HKA, LDFA, and MPTA angles between patients in the two groups before the operation (Table 1). The Pearson correlation coefficients, which measure the inter-observer consistency in measuring preoperative HKA, LDFA, and MPTA, are computed as 0.997, 0.961, and 0.950, respectively.

Constitutional Alignment before Surgery

The constitutional lower limb alignments of patients before receiving knee replacement were diverse. By comparing the distribution of CPAK phenotypes between two groups of individuals, we found that the frequencies of each type were similar. The commonest CPAK types were type II (16 (35.6%) cases in the MA group and 17 (35.4%) cases in the rKA group), followed by type I, type IV, and Type V (Fig. 2A,B). Merged CPAK demonstrated the same diverse distribution pattern (Fig. 2C).

Radiological Assessment of Surgery

The distribution of postoperative HKA was more concentrated in the range of $\pm 3^\circ$ of neutral in the rKA group (Fig. 3A,B). Detailed radiological evaluation was summarized (Table 2). After the operation, the mean HKA (in degrees) of the rKA group (0.8, 95% CI 0.0–1.6) was smaller than that of the MA group (2.0, 95% CI 0.8–3.2), although this difference was not significant ($P = 0.105$). We defined cases in which the difference between target HKA (0° for MA, patient-specific angles for rKA) and measured HKA was smaller

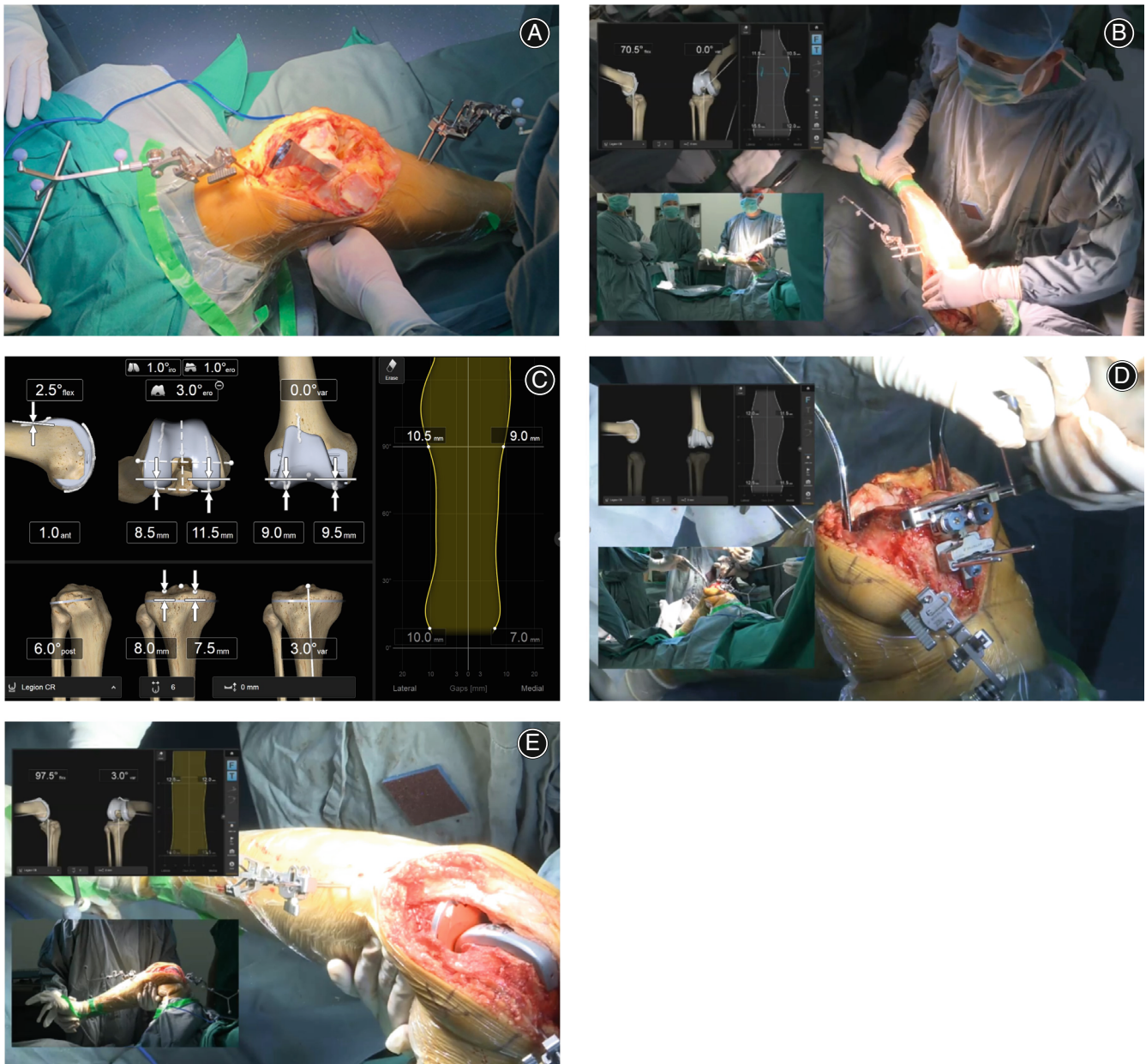


Fig. 1 Intraoperative operation of computer assisted navigation. (A) The tibial and femoral array was placed at desired location. (B) The leg was brought into maximum flexion, applying varus and valgus stress to test stability before surgical plan was made. (C) Surgical planning layout. (D) Cutting blocks with navigation plane tool was applied during bone resection. (E) Trial components were inserted and leg alignment, stability and medial/lateral gaps during rotation was finally assessed

than 1SD ($\leq 1.5^\circ$) as on-target cases, and for those with a difference greater than 2SD ($> 3^\circ$) were off-target cases. In the MA group, 21 cases (46.7%) fell into the safe zone of $\pm 3^\circ$ of neutral, and 12 cases (26.7%) achieved on-target MA, meanwhile, 24 cases (53.3%) were off target. In the rKA group, 41 cases (85.4%) fell into the range of $\pm 3^\circ$ of neutral. Thirty-four cases (70.8%) were on-target and six cases (12.5%) were off-target. In the rKA group, operations were

performed applying computer assisted navigation system. The verified accuracy (in degrees) was calculated according to the navigation system after the prosthesis was fitted. The verified accuracy of the rKA operation was 0.5 (95% CI 0.4–0.7). Actual accuracy (in degrees) was also calculated based on the image after surgery. The actual accuracy of the MA group (3.5, 95% CI 2.7–4.3) was significantly ($P < 0.001$) worse than that of the rKA

TABLE 1 Characteristics of patients at surgery in MA group and rKA group

Characteristics	MA group	rKA group	Test statistic ^b	P value ^c
Sample size	41	43		
Operation side ^a			0.225	0.635 ^d
L	20 (44.4%)	19 (39.6%)		
R	25 (55.6%)	29 (60.4%)		
Gender ^a			0.915	0.339 ^d
M	9 (22.0%)	6 (14.0%)		
F	32 (78.0%)	37 (86.0%)		
Age (years)	67.4 (6.2; 65.5, 69.4)	69.3 (6.4; 67.3, 71.2)	1.312	0.193
Height (m)	1.6 (0.06; 1.59, 1.63)	1.6 (0.07; 1.59, 1.63)	0.215	0.830
Weight (kg)	65.6 (8.7; 62.9, 68.4)	70.4 (9.0; 67.6, 73.2)	2.484	0.015
BMI (kg/m ²)	25.2 (3.0; 24.3, 26.2)	27.2 (3.2; 26.2, 28.2)	2.901	0.005
Preoperative alignment (°)				
HKA	7.8 (8.0; 5.3, 10.2)	8.3 (6.6; 6.4, 10.2)	0.360	0.720
LDFA	89.7 (5.5; 88.1, 91.4)	90.1 (3.3; 89.1, 91.0)	0.389	0.698
MPTA	85.0 (3.1; 84.1, 85.9)	85.0 (2.8; 84.0, 85.6)	0.289	0.773

Note: Values are presented as mean (standard deviation; 95% CI) unless indicated otherwise; ^at value for t-test and χ^2 value for χ^2 test; ^bUnpaired t-test, except; ^cFrequency (percentage); and; ^d χ^2 test.

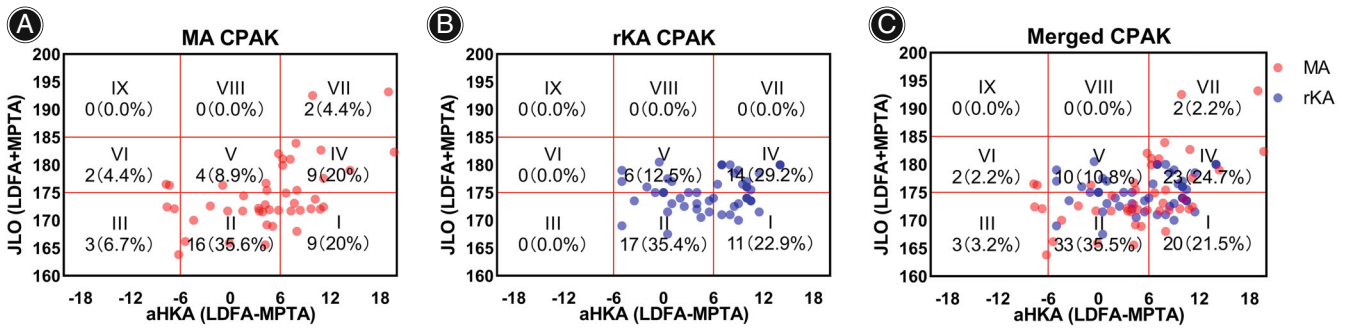


Fig. 2 Plots of Coronal Plane Alignment of Knee (CPAK) of both MA group and rKA group. Plots of arithmetic hip-knee-ankle angle (aHKA) against joint line obliquity (JLO) show the preoperative CPAK types of patients in (A) MA group and (B) rKA group. (C) Combination of two groups was plotted. LDFA, lateral distal femoral angle; MPTA, medial proximal tibial angle. JLO = LDFA + MPTA; aHKA = LDFA – MPTA, varus >0°, valgus <0°

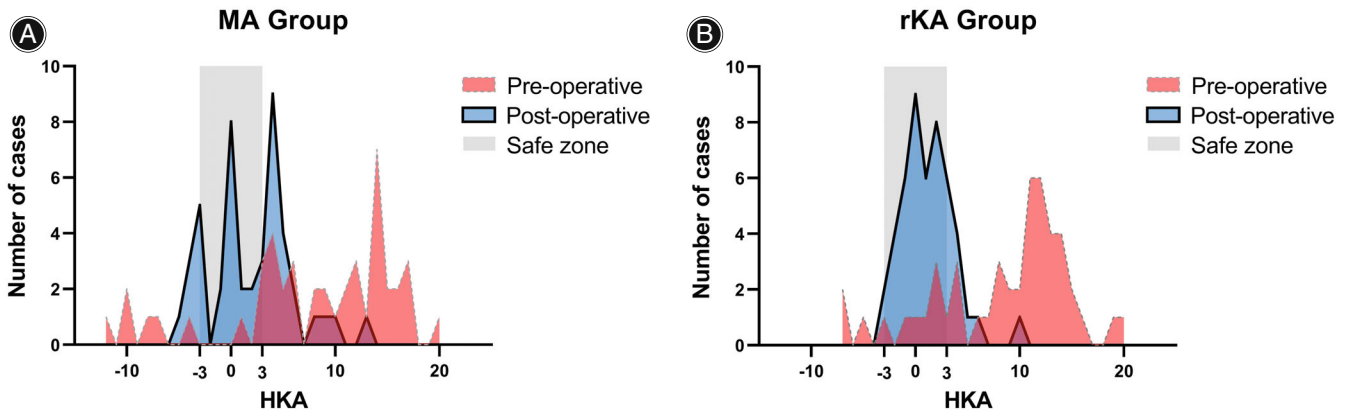


Fig. 3 Distribution of HKA angle before/after surgery in MA group and rKA group. The distribution of pre- and post-operational HKA angle of patients in (A) MA group and in (B) rKA group is plotted. Horizontal axis stands for HKA angle with varus >0° and valgus <0°; Vertical axis stands for number of cases with corresponding angle. The safe zone from –3° to 3° is marked as gray area.

TABLE 2 Comparison of alignments, surgical accuracy and precision of MA and rKA group

Postoperative alignment (°)	MA group (n = 45)	rKA group (n = 48)	Test statistic ^a	P value ^b
HKA	2.0 (4.0; 0.8, 3.2)	0.8 (2.7; 0.0, 1.6)	1.638	0.105
LDFA	91.5 (3.3; 90.5, 92.5)	90.5 (1.8; 90.0, 91.0)	1.777	0.079
MPTA	89.4 (2.5; 88.7, 90.2)	89.7 (1.9; 89.1, 90.2)	0.456	0.650
Safe zone ^c	21 (46.7%)	41 (85.4%)	15.69	<0.001 ^d
On-target ^c	12 (26.7%)	34 (70.8%)	18.12	<0.001 ^d
Off-target ^c	24 (53.3%)	6 (12.5%)	17.72	<0.001 ^d
Verified Accuracy (°)	–	0.5 (0.5; 0.4, 0.7)	–	–
Actual Accuracy (°)	3.5 (2.8; 2.7, 4.3)	1.5 (1.4; 1.1, 1.9)	4.301	<0.001
Precision ^e	4.0	2.0	3.541	<0.001 ^f

Note: Safe zone: HKA within $\pm 3^\circ$ of neutral; On-target: the difference between specific target value and measurement is within 1.5° ; Off-target: the difference between specific target value and measurement is larger than 3° ; Verified Accuracy = $|HKA_{\text{verification}} - HKA_{\text{plan}}|$; Actual Accuracy = $|HKA_{\text{final}} - HKA_{\text{plan}}|$; Precision was calculated as interquartile range of $HKA_{\text{final}} - HKA_{\text{plan}}$; Values are presented as mean (standard deviation; 95% CI) unless indicated otherwise; ^at value for t-test; χ^2 value for χ^2 test, and Z value for Westenberg test; ^bUnpaired t-test; ^cFrequency (percentage); ^d χ^2 test; ^eCalculated value; and; ^fWestenberg test for interquartile range equality.

TABLE 3 Perioperative records of patients in MA group and rKA group

	MA group	rKA group	Test statistic ^b	P value ^c
Operation time (min)	104.3 (17.9; 98.8, 109.8)	121.7 (15.4; 117.0, 126.4)	4.862	<0.001
Tourniquet time (min)	64.5 (10.0; 61.5, 67.6)	83.9 (10.2; 80.9, 86.9)	9.202	<0.001
Length of Stay (day)	9.8 (4.6; 8.3, 11.2)	7.5 (1.5; 7.0, 7.9)	3.195	0.002
Hemoglobin (g/L)				
Day 0	136.7 (13.7; 132.5, 140.9)	136.9 (11.2; 133.6, 140.2)	0.099	0.921
Day 1	124.8 (18.3; 119.2, 130.3)	126.4 (10.5; 123.3, 129.5)	0.514	0.609
Day 3	118.1 (13.6; 113.9, 122.3)	117.1 (9.2; 114.4, 119.8)	0.412	0.682
Hematocrit (%)				
Day 0	40.0 (7.3; 25.7, 54.3)	39.5 (7.1; 25.6, 53.4)	0.455	0.961 ^d
Day 1	36.2 (7.2; 22.1, 50.3)	37.1 (7.0; 23.4, 50.8)	0.861	0.928 ^d
Day 3	35.0 (7.1; 21.1, 48.9)	34.8 (6.9; 21.3, 48.3)	0.289	0.984 ^d
Complications ^a	0	0	–	–

Note: Operation time: total operation time of TKA recorded in surgical system; Tourniquet time: The length of time when tourniquet was applying; Day 0: the day before surgery; Day 1: the day after surgery; Day 3: three days after surgery; Complications: cases with aseptic loosening, joint instability, periprosthetic infection and surgical site infection. Values are presented as mean (standard deviation; 95% CI) unless indicated otherwise; ^aFrequency; ^bt value for t-test and χ^2 value for χ^2 test; ^cUnpaired t-test; ^dZ test for two proportions.

group (1.5, 95% CI 1.1–1.9). The precision of the rKA group (interquartile range 4.0) was significantly ($P < 0.001$) better than that of the MA group (interquartile range 2.0) (Table 2). The Pearson correlation coefficients were used to measure the inter-observer consistency in measuring postoperative HKA, LDFA, and MPTA, which were computed as 0.993, 0.982, and 0.963, respectively.

Perioperative Record and Complications

Both operation time and tourniquet time were shorter in the MA group compared to the rKA group. In terms of blood loss, there was no significant difference in both hemoglobin and hematocrit between the two groups of patients from the day before the operation to 3 days after the operation. For those patients in the MA group, the

length of hospitalization was significantly longer than that of patients in the rKA group. During the 6-months follow-up, complications, including aseptic loosening, joint instability, periprosthetic infection, and surgical site infection, were not observed in both groups (Table 3).

Short-term Outcomes

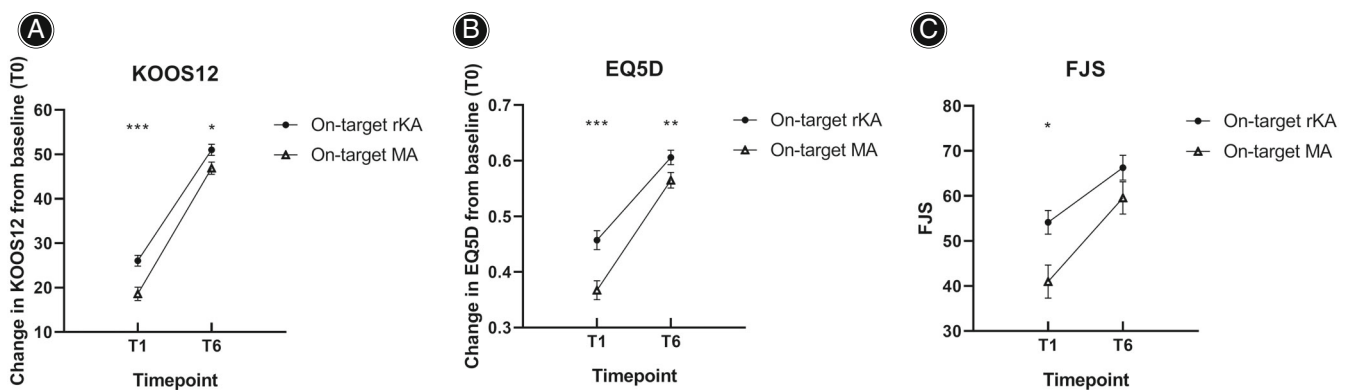
We presented the results from the GEE models that examined the effects of alignment and other demographic characteristics and clinical measures on each of the PROMs (Table 4) as well as each estimated PROMs for subjects with on-target rKA and on-target MA at 10 days (T1) and 6 months (T6) after the operation (Table 5). We found that, after adjusting for potential effects of age, sex, BMI, operation and tourniquet time, length of stay, change in HKA,

TABLE 4 Parameter estimates, 95% confidence intervals, and p-values for GEE models that assessed the effect of alignment on PROMs after adjusting for demographic characteristics and clinical measures

Effect	Change in KOOS12 from TO			Change in EQ5D from TO			FJS		
	Estimate (95% CI)	Z value	P-value	Estimate (95% CI)	Z value	P-value	Estimate (95% CI)	Z value	P-value
Intercept time	18.607 (15.691, 21.523)	12.51	<0.001	0.367 (0.334, 0.400)	21.56	<0.001	40.965 (33.752, 48.178)	11.13	<0.001
T6	28.288 (25.373, 31.203)	19.02	<0.001	0.196 (0.172, 0.220)	16.13	<0.001	18.615 (15.816, 21.414)	13.03	<0.001
Alignment rKA	7.446 (3.706, 11.186)	3.90	<0.001	0.090 (0.049, 0.131)	4.27	<0.001	13.161 (4.717, 21.605)	3.06	0.002
Time × alignment									
T6 × rKA	-3.324 (-7.091, 0.443)	-1.73	0.084	-0.049 (-0.082, -0.016)	-2.85	0.004	-6.486 (-10.208, -2.764)	-3.42	0.001
Age	-1.768 (-2.489, -1.047)	-4.80	<0.001	-0.012 (-0.022, -0.002)	-2.65	0.008	-2.405 (-3.924, -0.886)	-3.10	0.002
Sex									
Female	-1.283 (-3.129, 0.563)	-1.36	0.173	-0.016 (-0.040, 0.008)	-1.38	0.168	-0.715 (-5.192, 3.762)	-0.31	0.754
BMI	0.081 (-0.711, 0.873)	0.20	0.842	-0.004 (-0.012, 0.004)	-0.87	0.385	1.045 (-0.374, 2.464)	1.44	0.149
Operation time	-0.831 (-2.146, 0.484)	-1.24	0.216	-0.010 (-0.022, 0.002)	-1.56	0.120	0.803 (-1.870, 3.476)	0.59	0.556
Tourniquet time	0.225 (-1.123, 1.573)	0.33	0.744	0.002 (-0.014, 0.018)	0.27	0.791	-0.649 (-4.122, 2.824)	-0.37	0.714
Length of stay	-0.342 (-1.351, 0.667)	-0.66	0.507	-0.005 (-0.017, 0.007)	-0.77	0.443	0.600 (-2.246, 3.446)	0.41	0.679
Change in HKA	0.639 (-0.296, 1.574)	1.34	0.181	-0.001 (-0.011, 0.009)	-0.23	0.815	-1.561 (-3.421, 0.299)	-1.64	0.100
Target									
Not on-target	2.752 (0.108, 5.396)	2.04	0.041	0.032 (0.007, 0.057)	2.56	0.011	1.956 (-4.128, 8.040)	0.63	0.529
Target × alignment									
Not on-target × rKA	-5.744 (-9.307, -2.181)	-3.16	0.002	-0.052 (-0.089, -0.015)	-2.76	0.006	-0.586 (-7.952, 6.780)	-0.16	0.876
Baseline KOOS12	-8.196 (-9.431, -6.961)	-13.00	<0.001	0.005 (-0.007, 0.017)	0.79	0.427	0.598 (-1.666, 2.862)	0.52	0.605
Baseline EQ5D	0.876 (-0.245, 1.997)	1.53	0.125	-0.195 (-0.207, -0.183)	-32.44	<0.001	1.418 (-0.961, 3.797)	1.17	0.243

TABLE 5 Estimated PROMs and 95% confidence intervals at T1 and T6 for subjects with on-target rKA and on-target MA based on GEE models that adjusted for demographic characteristics and clinical measures

	On-target rKA	On-target MA	Z Value	P-value
Estimated change in KOOS12 from baseline				
T1	26.053 (23.658, 28.448)	18.607 (15.691, 21.523)	3.90	< 0.001
T6	51.017 (48.567, 53.467)	46.896 (44.187, 49.605)	2.28	0.023
Estimated change in EQ5D from baseline				
T1	0.457 (0.424, 0.490)	0.367 (0.334, 0.400)	4.27	< 0.001
T6	0.606 (0.581, 0.631)	0.565 (0.538, 0.592)	2.58	0.010
Estimated FJS				
T1	54.126 (48.932, 59.320)	40.965 (33.750, 48.180)	3.06	0.002
T6	66.256 (60.809, 71.703)	59.581 (52.486, 66.676)	1.64	0.102

**Fig. 4** Visualization of short-term clinical outcomes of patients in different timepoints. The (A) changes in estimated KOOS12 from baseline (T0), (B) changes in EQ5D from baseline (T0) and (C) estimated FJS at different timepoints are plotted. T0: before surgery; T1: 10 days after surgery; T6: 6 months after surgery. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

whether the case was on target, baseline KOOS12, and baseline EQ5D, there was a statistically significant difference in each of the PROMs between subjects with on-target rKA and those with on-target MA at T1. The estimated change in KOOS12 from baseline to T1 for subjects with on-target rKA was 26.053 (95% CI 23.658–28.448) and that for subjects with on-target MA was 18.607 (95% CI 15.691–21.523), resulting in a statistically significant difference ($P < 0.001$) in the change in KOOS12; the same trends were also observed in EQ5D. The estimated FJS at T1 for subjects with on-target rKA was also higher than that for subjects with on-target MA. Similar observations can also be made for T6.

We also found some other demographic characteristics and clinical measures associated with the outcomes of interest. For example, when there was a one standard deviation increase in age (about 6 years), it was estimated that the change in KOOS12 after the operation would be 1.768 (95% CI 1.047–2.489, $P < 0.001$) lower, and the change in EQ5D and the FJS after the operation would also be lower. In addition, the baseline KOOS12 was found to have a statistically significant effect on the change in KOOS12 from baseline (estimate = -8.196 , 95% CI -9.431 to -6.961 , $P < 0.001$), and the baseline EQ5D was also found to have a statistically

significant effect on the change in EQ5D from baseline. Note that, the covariates of target and target by alignment interaction were included in the model to account for potentially different effects between rKA and MA that are not on target compared to their on-target counterparts. Interestingly, subjects with MA that is not on-target were found to have 2.752 (95% CI 0.108–5.396, $P = 0.041$) higher increase in KOOS12 after operation, 0.032 (95% CI 0.007–0.057, $P = 0.011$) higher increase in EQ5D after operation, and 1.956 (95% CI -4.128 to 8.040, $P = 0.529$) higher FJS compared to those with on-target MA. Some visualizations for the paths of KOOS12, EQ5D, and FJS were also presented (Fig. 4A–C).

Discussion

In this study, we adopted a patient-specific rKA strategy based on phenotypes analysis. We demonstrated that the computer assisted navigation provided adequate accuracy and precision in rKA-TKA and rKA-TKA had priority over MA-TKA in short-term clinical outcomes.

Rationale of Adopting rKA Strategy

The key to the success of TKA is to provide a stable and comfortable kinematic by achieving proper alignment and

balanced mediolateral gaps and correcting joint deformities.²⁰ As the earliest and most widely used strategy, mechanical alignment (MA) fulfills the need to improve prosthetic survival at the early stage when the quality of the prosthesis remained poor.²¹ However, more and more evidence indicates that MA-TKA fails to restore preoperative kinematics.²² Hence, with the full development of prosthetic materials, surgeons began to focus on the phenotypes of the knee of the population. Several studies have revealed the diversity of knee phenotypes, therefore the neutral lower limb alignment pursued by the traditional MA does not conform to the constitutional anatomy of individuals.^{23–25} Among different classifications, we regard the CPAK classification proposed by MacDessi *et al.*¹⁷ as a practical system since the nine classifications defined based on mathematical formulas have good clinical applicability. In our population, the preoperative CPAK distribution was similar to that of authors that phenotype I, II, and IV were three main types, rather than type V, of which preoperative alignment was as neutral as the alignment that the MA strategy pursued. Hence, this was convincing enough for us to choose a more individualized strategy. KA seemed to be an option for us because it restores the same anatomy as preoperative knees and does not alter original gaps and ligament laxity.²⁶ We retrospectively analyzed the lower limb alignments of the MA group and the mean preoperative HKA was 7.8°, which was out of the commonly accepted safe range of $\pm 3^\circ$. This supported our choice to use the rKA strategy so that we could reduce soft tissue release and partially restore the constitutional kinematics without potentially sacrificing long-term survival.

Navigation Is Capable for rKA-TKA with Accuracy, Precision and Safety

To accurately implement rKA alignment, computer assisted navigation was applied to formulate the individualized alignment goal for each patient, based on the preoperative alignment. Based on the previous surgical experience of our center, there was an error of about 0.5° in the navigation system. This meant even if we strictly followed the guide during operation, there was still an average error of 0.5° from the planned value when performing alignment verification after the prosthesis was installed. The same phenomenon was observed in this study that the verified accuracy of navigation was 0.5°. Therefore, we recommend in order to improve the rKA-TKA success rate with navigation, the planned HKA should not exceed $\pm 2.5^\circ$ to account for errors in navigation assisted surgery. This preoperative planning strategy was regarded as restricted rKA (rrKA). In the rKA group, the application of navigation improved the accuracy and precision compared to the conventional method in the MA group, which was widely reported by other publications.^{27–29}

We evaluated the radiological outcomes of two groups. Before surgery, the distribution of HKA in both groups was scattered and the varus of more than 3° was predominant. To determine whether the targeted alignment was achieved for each case, the difference between targeted

HKA and postoperative HKA was calculated. The ratio of on-target cases was higher in the rKA group compared to the MA group ($P < 0.001$), and the off-target rate was lower ($P < 0.001$). This off-target rate of navigation assisted TKA (rKA group, 12.5%) was similar to the results reported by Shah *et al.*¹⁶ In terms of keeping postoperative HKA within a $\pm 3^\circ$ safe zone, the rKA group was also superior to the MA group ($P < 0.001$). To summarize, in the aspect of postoperative radiology assessment, computer assisted navigation is capable to achieve rKA-TKA with high accuracy and precision.

We found that the operation time and tourniquet time significantly increased in the rKA group than in the MA group, and this was consistent with some other studies.^{28,30} In a study based on a large sample size, Sekimura *et al.* claimed that the operation time of navigation TKA was longer than the traditional TKA at the beginning, and later developed to be shorter by 2018.³¹ In our opinion, the increase in time was due to: (i) there were more steps in navigation TKA, for instance, planning, registration, verification, etc. which prolonged the operation time; and (ii) there was a learning curve when applying new techniques so that the time was able to be shortened in following cases. The reasons that surgeons cared about operation time were due to the increase in time associated with infection and more blood loss. We, therefore, investigated the blood loss by acquiring the value of hemoglobin and hematocrit from the day before the operation (day 0) to three days after (day 3). There was no significant blood loss between these two groups, and this was not consistent with studies indicating navigation could reduce the blood loss and transfusion rate.^{32–34} In both groups, no TKA-related complication was reported during the 6-month follow-up.

rKA-TKA Can Improve Short-term PROMs

In this ambispective study, we had been not able to apply navigation in the MA group, so the accuracy and precision of surgery were different in the two groups. Therefore, we used GEE models to adjust for this difference in accuracy and precision, along with some other demographic characteristics (i.e., age, sex, operation sides, etc.) and clinical measures that may have potential effects on PROMs. In addition, the correlation between the measurements taken on the two knees of the bilateral TKA cases can be significantly larger than the correlation between the measurements taken on two separate patients, and GEE models are also capable of adjusting for such correlation in the analysis.^{35,36} One of the most important discoveries was that when surgery was precisely performed to achieve the target (i.e., MA or rKA) in both groups, those patients who received rKA-TKA had a better short-term performance than those with MA-TKA. This made up for deficiencies in the design of this ambispective study, and this was also in line with the purpose pursued by the rKA strategy. In our opinion, this improved performance was due to the limited soft tissue release and correction of severe preoperative deformities, resulting in better knee kinematics. The higher

KOOS12 and EQ5D represented less pain and discomfort, and higher FJS may suggest a higher willingness to exercise. We believed these improvements were critical for recovery, meaning that patients can start ROM and other functional exercises earlier, which would therefore reduce the incidence of postoperative deep vein thrombosis and allow patients to return to normal life earlier.^{37,38} We also found that the outcomes of those with MA that were not on-target were better than those with on-target MA. This was because, in our MA group, the alignments of those not on-target cases were inadvertently closer to the goal of rKA or KA. This might suggest the superiority of rKA over MA from another perspective. Greater BMI has been widely identified as a risk factor for osteoarthritis, but we did not observe this effect on our results of PROMs. It was not surprising that those more aged people had a poorer prognosis, and those who had worse preoperative knee conditions can benefit more from the surgery.

Strengths and Limitations

The strength of this study lies in the comprehensive data collection and rigorous statistical analysis, which provided a basis for clinical decision-making in the application of navigation-assisted rKA-TKA. This study has some limitations: (i) we were not able to retrospectively include more patients in the MA group because of limited cases in our center; and the sample size was also not large enough for us to match patients between two groups in the study; (ii) navigation was only applied in the rKA group but not in the MA group. However, the GEE model is capable of taking into account the confounding effect of different surgical techniques^{35,36}; and (iii) we only followed the patients for 6 months, so this study was not able to provide further evidence for longer clinical outcomes.

Based on this study, we recommend applying navigation in rKA-TKA to improve short-term outcomes. In the future, larger sample size will be studied to establish knee phenotypes based on our population, and the prognosis of patients with different phenotypes will be investigated to provide a more detailed flow chart for preoperational planning to implement real individualized rKA-TKA and improve the prognosis.

Conclusion

The study found that computer assisted navigation achieved the level of accuracy required to perform rKA-TKA. Within

the knee phenotypes demonstrated in this series, rKA-TKA offered significantly better short-term functional outcomes than MA-TKA.

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Author Contributions

All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Ruichen Ma contributed in conceptualization, data curation, formal analysis, investigation, methodology, validation, visualization, writing original draft and editing. Xi Chen contributed in conceptualization, data curation, funding acquisition, methodology, supervision and draft review. Haolin Li contributed in formal analysis, methodology, draft review and editing. Yiyou Wang, Songlin Li and Shanni Li contributed in investigation, methodology, draft review and editing. Wenwei Qian contributed in conceptualization, methodology, funding acquisition, supervision and draft review.

Conflict of Interest

The authors have no conflicts of interest relevant to this article.

Ethics Statement

This study involving human participants was reviewed and approved by the Institutional Review Board of Peking Union Medical College Hospital. The study was undertaken with the understanding and written informed content of each participant.

Authorship Declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

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