Aus der Klinik für Orthopädie und spezielle orthopädische Chirurgie

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# Match-paired study to assess influence of Kinematic versus Mechanical Alignment in Total Knee Replacement

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Hiermit erkläre ich, die Dissertation mit dem Titel "Match-paired study to assess influence of Kinematic Versus Mechanical Alignment in Total Knee Replacement" eigenständig angefertigt und keine anderen als die von mir angegebenen Quellen und Hilfsmittel verwendet zu haben.

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# List of Abbreviations

| | |
|---|---|
| 3D | three-dimensional |
| AP | anterior-posterior |
| CAOS | computer assisted orthopedic surgery |
| CR | cruciate retaining |
| DLFA | distal lateral femoral angle |
| EQ-5D | EuroQOL – 5 Dimensions |
| FJS | Forgotten Joint Score |
| HKA | hip-knee-ankle |
| JLCA | joint line convergence angle |
| KA | kinematical alignment |
| KSS | Knee Society Score |
| KOOS | Knee Injury and Osteoarthritis Outcome Score |
| LDFA | lateral distal femoral angle |
| MA | mechanical alignment |
| MP | medial pivot |
| MPTA | medial proximal tibial angle |
| OKS | Oxford Knee Score |
| PFJ | patellofemoral joint |
| PSI | patient specific implant |
| QOL | quality of life |
| RCT | randomized control trials |
| ROM | range of movement |
| RSA | radiostereometric analysis |
| TKA | total knee arthroplasty |
| VAS | visual analogue scale |
| UCLA | University of California Los Angeles Activity Score |
| WOMAC | Western Ontario and McMaster Universities Osteoarthritis Index |

# 1 Introduction

Total Knee Arthroplasty (TKA) has been performed widely since the 1970s. It is successful in relieving pain and improving knee function in people with advanced arthritis; however, patient satisfaction following TKA surgery remains inferior in comparison to hip arthroplasty. Modern intraoperative assistive technologies (navigation, CAOS–computer assisted orthopedic surgery, PSI—patient specific instrumentation, and robotics) that have been combined with the mechanical alignment concept have failed to provide a solution for residual symptoms and higher rates of dissatisfaction in patients with knee replacements (Bourne et al. 2010; Nam et al. 2014). This has occurred despite good functional outcomes and excellent longevity of components. Long-term outcomes suggest that a number of factors contribute towards improving functional outcomes and satisfaction. One such factor is the type of alignment option selected for performing a TKA. The most widely used alignment option is the mechanical alignment technique; recently, more surgeons have been questioning whether this is the gold standard for TKA (Spencer et al. 2007; Lützner et al. 2013; Parvizi et al. 2014; Rhee et al. 2019).

The KA technique (Howell et al. 2008; Howell et al. 2013) aims at restoring the native joint line. The KA technique allows co-alignment of the rotational axis of the femoral components with those of the native femur and tibia to restore motion, physiological compartment forces, and joint laxities with minimal ligament release. Furthermore, KA was developed as a concept that aims to reconstruct 3D joint line obliquity respecting natural knee kinematics without compromising soft tissue laxity with unnecessary ligament releases and nonphysiological orientations of components (Eckhoff et al. 2005; Howell et al. 2008).

## 1.1 Differences in clinical outcome between KA TKA and MA TKA

A key goal of modern arthroplasty has been to mimic the native knee phenotype, the soft-tissue envelope, and natural joint laxity (Eckhoff et al. 2005; Rivière et al. 2017). Over the past decades, several advancements (including alignment technique, kinematics of the flexion extension axis and medial pivot systems) have provided a fresh insight into achieving higher functional outcomes and satisfied patients.

The first published study comparing KA with mechanical alignment was by Dossett (2012). The author reported on 82 knees with a 6-month follow-up performed with PSI instruments compared with conventional measured resection with CR fixed-bearing implants. No releases were performed in the KA group. Authors described the superiority of KA through the Oxford Knee Score (OKS) $p = 0.001$, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) $p = 0.001$ and Knee Society Score (KSS) $p = 0.001$. Further analysis based on radiological outcomes, demonstrated that the joint line obliquity showed significant differences between groups, whereas, compared to the MA group, the KA group had a more oblique joint line orientation angle (JLOA) ($p = 0.001$). The next RCT (Dossett et al. 2014) from the same author included 88 patients who were compared with no restriction on deformities. The same PSI system was applied for the KA group and conventional measured resection for MA. No releases were performed in the KA group.

Statistically significant differences were found in the OKS group ($p = 0.005$), WOMAC ($p = 0.005$), and KSS ($p = 0.004$).

The odds ratios for pain-free status after 2 years in the WOMAC and OKS groups were 52% and 39%, respectively, in the KA group compared to 18% and 16%, respectively, in the MA group ($p = 0.001$ and $p = 0.02$). Analyzing patellofemoral compactions, the authors concluded that there was no difference between the groups ($p = 1.0$).

Calliess (2017) followed a group of 200 randomly assigned patients for 1 year, comparing PSI KA and conventional measured resection MA. Both groups were treated with CR fixed-bearing implants. There were restrictions imposed on preoperative valgus/varus deformities (knees with more than +/- 10° deformities were excluded) and on the angles of DLFA (distal lateral femoral) and MPTA (medial proximal tibial) (values for both between 86° and 92°). No releases were made in the KA group. Improvements in the WOMAC ($p = 0.001$) and KSS ($p = 0.02$) underlined statistically significant differences between groups, favoring KA.

Waterson (2016) randomized 71 patients into 36 KA vs 35 MA groups, with PSI technology and conventional measured resection, respectively. Patients with severe deformities and flexion contractures were excluded (restrictions were set at +/- 7°). The authors concluded that there was no significant advantage. Only exceptions were early functional improvement (first 6 weeks) of KSS score and peak torque of the quadriceps in the kinematically aligned group ($p = 0.05$).

Young (2017) reported a double-blinded randomized study with 99 TKAs. Comparisons were performed on 49 KA TKAs and 50 MA TKAs with PSI technology and navigation, respectively. This was the second study showing similar outcomes; nevertheless, KA showed a small functional advantage over MA, albeit one that was not statistically significant.

The improvement in the Forgotten Joint Score (FJS) in both groups was 29 points, yet the mean FJS in the KA group was higher (KA group 69 to MA group 66).

The similarity between the results can be partially explained by the fact that ligamentous releases were performed if necessary, to achieve symmetric balance in flexion and extension, and the kinematic protocol was frequently changed. After 2 years of follow-up, Young et al. concluded there was no difference in functional outcomes between groups.

In contrast, Matsumoto et al. (2017) in their RCT reported better functional outcomes in a group of 30 KA patients compared with 30 MA patients. The cohorts were operated on with computer-assisted orthopedic surgery (CAOS), and both mobile-bearing and fixed-bearing implants were used. The researchers compared new KSS outcomes as well as ROM and reported a statistically significant improvement of KA patients in the objective score ($p = 0.003$) and functional activities ($p = 0.027$) measured by the Knee Injury and Osteoarthritis Outcome Score (KOOS).

McEwen (2019) reported in a double-blinded RCT including 41 patients (82 TKAs) who were operated on bilaterally and simultaneously using navigation with KA and MA principles, respectively. The authors used hybrid fixation cementless femur and cemented the tibia with a CR implant in all patients. Demographically, there were no valgus joints included in the study, and, consequently, the results should be interpreted as varus and neutral preoperative joint deformity. Preference for KA TKA compared to MA TKA ($p = 0.03$) despite the equivalence of functional outcomes suggest a ceiling effect in the PROMs used.

Laende (2019), employing a radiostereometric analysis (RSA) comparing PSI KA and CAOS MA, reported in RCT no statistical significance in secondary outcomes (UCLA, OKS, VAS), although PROM outcomes were higher in the KA group than in the MA group.

In 2020 (French et al. 2020) published a single-surgeon study comparing 46 kinematically aligned medial pivot and 44 kinematically aligned cruciate-retaining TKAs performed with conventional instruments and followed an average of 1 year. Both groups of patients improved significantly. The authors noted that the FJS and KOOS subscore of life quality (QOL) were superior in the medial pivot group. This result was shown to be statistically significant. This was the first report of the comparison between different implants used with caliper-measured KA technique. Other scores such as the OKS, WOMAC, UCLA Activity scale, visual analogue scale (VAS) and EuroQOL–5 Dimensions (EQ-5D) had similar outcomes

Niki (2018) reported better functional outcomes in the KA group in the case-control setting. Comparing 45 KA TKA and 45 MA TKA patients by using the KSS as an outcome measure, the authors concluded that superior functional outcome scores in the KA group ($p = 0.047$) were related to joint line modification, but not directly to better satisfaction, in this particular group of patients. Retrospective case-controlled study (Blakeney et al. 2019) published as secondary outcomes better KOOSs in the KA group compared to the MA group (74 vs 61) ($p = 0.034$).

Meta-analysis and systematic reviews reported differences in kinematically and mechanically aligned TKA with special focus on primary and secondary outcomes. Courtney and Lee (2017) reported in their meta-analysis of 4 RCTs that the combined KSS in the patient group treated with KA was higher than scores in the MA group (mean difference 9.1; $p < 0.001$). Similarly, Takashi et al. (2018) recently showed in their study of 5 RTCs (4 with PSI and one with navigation) that patients with KA TKA had better primary functional outcomes than patients treated with MA TKA. The authors reported higher functional results on the WOMAC ($p < 0.0001$) and OKS ($p = 0.03$) combined with the KSS ($p < 0.0001$) and Knee Function Score ($p = 0.0007$). However, the KSS ($p = 0.3$) and EQ-5D ($p = 0.57$) showed no statistical significance between groups.

The study of Woon et al. (2018) is the only meta-analysis where functional outcomes were no different between both types of alignment. They reported only RCTs performed with PSI technology (Woon et al. 2018).

Li (2018) showed that the WOMAC ($p < 0.001$), function section of the KSS ($p = 0.03$), and the OKS ($p = 0.03$) were significantly different in favor of KA alignment, but there was consequently no difference in the KSS ($p = 0.13$) and VAS for pain ($p = 0.2$). Recently, Xu (2019) published a systematic review of 7 RCT studies and 1 case series study. The authors reported a shorter operation time and better functional outcomes in functional KSS ($p = 0.004$) and combined KSS ($p = 0.002$) in the KA group of patients.

## 1.2 Evaluation of Radiological Outcomes: Neutral Limb Alignment with Oblique Joint Lines in Patients with KA TKA

Radiological outcomes show a difference between KA and MA joint line orientation and varus/valgus position of implanted tibial and femoral implants, but no statistically significant difference in the overall hip-knee-ankle (HKA) axis. KA HKA axis is likely to be more similar to the normal distribution of limb alignments in the general population.

Recently, there were reports about the dangers of aligning the tibia in a more varus position, measured in partially inappropriate radiographic and experimental biomechanical surroundings (Nakamura et al. 2017; Teeter et al. 2018). Large extraarticular deformities, high BMI, and anatomical variations present a concern regarding varus of the tibial component in MA TKA (Ritter et al. 2011; Abdel et al. 2015). Such concerns contrast with former reports about long-term survivorship in outlier groups (Matziolis et al. 2010; Magnussen et al. 2011; Abdel et al. 2018). However, these conflicting reports should be solely translated to MA. It should be noted that axial irregularities, flexion/extension deficits, and spine, hip and ankle pathology influence true limb measurements and therefore make the appearance of a long leg 2D radiologically difficult to reproduce. These findings could not be generalized to the KA technique. Van Hamersveld et al. (2019) employed a radiostereometric analysis (RSA) with the aim of reconstructing constitutional varus via an adjusted alignment technique and showed that MA patients are at higher risk of aseptic loosening. Hence, Laende et al. (2019) reported no correlation of migration and component positions in their RSA study on differences in PSI KA and navigated MA. In their 2-year follow-up, the authors reported that if KA is out of a “safe range”, there is likely no longitudinal tibial migration from significance for early component loosening. All these findings support the opinion that 2D coronary alignment should be seen as only a tool and is not as reliable for predicting outcomes.

These studies corroborate the principles of KA, which is the reconstruction of limb alignment, biomechanical properties and kinetics in joint and load distribution in joint lines.

KA does not aim to achieve a neutral 180° axis. Case series showed that kinematically aligned PSI had fewer varus limb and knee outliers than mechanically aligned PSI and conventional TKA.

The results of 220 PSI surgeries on 216 patients with 10 years follow-up of their knees revealed that 73% of knees (with the anatomic angle as measurement) and 83% of limbs were in range (Howell et al. 2018).

Similar results were reported by Nunley (2012) 44 % and by Almaawi (2017) 49 % , but higher than the 22% observed by Waterson (2016) and the 35% by Young (2017). On the other hand, there was no difference in overall limb alignment between KA and MA. Although only MA targeted the neutral axis, numerous studies reported no difference in mean HKA angles. There was only one RCT that showed a significant difference in mean values between the KA and MA groups, finding a 2° difference in the overall HKA alignment (Matsumoto et al. 2017).

It was Dossett et al. (2014) who reported no statistically significant difference between the alignment of a limb (HKA) and the anatomical axis. However, joint line inclination, tibial, and femoral component differences showed significant differences. The authors found that the tibial component had of 2.2 degrees more varus and femoral component 2.1 degrees more valgus. Several studies suggest similar findings with joint line obliquities of 1° (Hutt et al. 2016), 0.9° (McEwen et al. 2019) and in double leg stance 1.1° (Matsumoto et al. 2017) in KA patients, which is actually a real target in KA. Recently, in RCT, McEwen et al. (2019) reported bilateral simultaneous KA and MA TKA paired side-to-side difference values of 2.3 degrees varus and 1.5 degrees valgus in MPTA and DLFA, respectively. Similarly, one retrospective case-control study (Blakeney et al. 2019) showed a 2.5-degree difference between MPTA and DLFA in KA and MA.

The meta-analysis of Takashi (2018) reported radiologically clear differences in obliquity of the joint line between both types of alignment. This finding is in accordance with the findings of Lee et al. (2017) that the joint line is oriented more parallel to the floor, while the overall limb alignment in the HKA axis is similar between groups. Studies from Niki (2018) and Blakeney et al. (2019) underline that the orientation in varus knee joints shifts the joint line in an oblique manner in most knees, reduces the adduction moment, and improves ROM (flexion), resulting in joint lines that are more natural comparing one-leg to both-legs radiographs in stand and bear weight centrally through the knee compared with the corresponding positions in patients who undergo a mechanically aligned TKA.

## 1.3 Long-term results, implant survival rates, and rates of complications in kinematically aligned TKA

KA is a highly reliable and reproducible technique for high-volume surgeons with no distinctive complication rate in the short term. Long-term outcomes are likely to be predicted from good functional results in follow-ups up to two years (Williams et al. 2013).

Until now, few long-term results of KA have been reported. Currently, there is one long-term study of implant survivorship complications and revision rates for the current generation of KA TKA. Howell et al. (2018) showed that the patients treated with KA without restricting indications regarding limb alignment and joint line obliquity benefit through better functional outcomes and diminished risk of revision compared with similar cohorts of patients in a single-surgeon case series operated with MA (Bonner et al. 2011; Abdel et al. 2018)

In their study on 220 consecutive patients, Howell et al.(2018) reported implant survival of 98.5%, with only one tibial loosening. The reasons for tibial loosening are not comparable with MA (varus overload caused by changes in the soft-tissue balance inherently characteristic of MA) but have their own rationale for erroneously overcorrecting the anatomical tibial slope for more than 7° and posterior overload of the tibial component.

Reported midterm outcomes have indicated highly favorable results with PSI instrumentation (Howell et al. 2015). In this study, the authors concluded that varus alignment of a limb and tibial implant does not influence the high functional outcome and implant survivorship of 208 knees at a mean follow-up of 6 years. The implant survivorship of 98% and very low revision rate are comparable to those of mechanically aligned TKA reported by a knee arthroplasty registry for the same implant design at six years. Supporting the results from the designer of the concept (Labek et al. 2011), numerous short-term follow-up RCTs in the literature show that early results are good prognostic factors for long-term outcomes (Williams et al. 2013).

The rates of major (removal or exchange of components) and minor complications in current publications comparing KA and MA aligned TKAs are few and not significantly different between both techniques. Reported major complications related to KA in studies are infrequent. Usual concerns include patellofemoral issues and tibial loosening. Hence, the rates of adverse effects on patellofemoral joint (PFJ) and the revision rates for any cause were similar between KA and MA (Klasan et al. 2020).

Concerns in KA are partly focused on patellofemoral complications. Although biomechanical studies (Rivière et al. 2018; Lozano et al. 2019) show evidence for more physiological tracking of KA, a deeper understanding of KA in combination with morphotypic variability and dysplastic properties in PFJ (Rivière et al. 2018) remains a focus of attention. The PFJ complications were reported as rare and showed no difference from MA in frequency.

There are published reports (Nedopil et al. 2017a) of rare complications (less than 0.4% of patients operated with PSI KA TKAs) with patella subluxations with different implants not related to previous subluxation of the valgus knee functional phenotype. The authors concluded in a case-match paired study that femoral component flexion that is on average 5° more than the physiological value leads to such outcomes. The reasons for such rare complications are more error in the operative technique and, most likely, the use of specific dome-shaped implants.

The same could be claimed for 1.6% aseptic loosening after 12 years of KA, which coincides with an excessive tibial slope of more than 7° in the control group (Nedopil et al. 2017b).

In RCTs, major complications after calipered KA TKA are infrequent and do not contribute to a higher revision rate or, in any case, influence the safety of the procedure in short follow-up (Dossett et al. 2014; Calliess et al. 2017; Young et al. 2017).

One of the studies in which PSI implants were used had multidirectional instability as the reason for revision (Calliess et al. 2017), but the revision rate was not different from MA. Similarly, published systematic reviews and a meta-analysis (Lee et al. 2017; Takahashi et al. 2018; Woon et al. 2018; Xu et al. 2019) have reported no difference in complication rates in a maximum short-term follow-up period of $\leq$ 2 years.

## 1.4 Aims of the thesis

This case-controlled study aims to assess 1-year outcomes and radiological results after kinematical alignment medial pivot TKA and compare them to mechanical alignment medial pivot TKA. The end goal is to achieve an oblique joint line without ligaments release and preserving soft tissues constitutional properties are the cornerstone of kinematically aligned TKA. Integrating KA technique with medial pivot design is a possible option to improve functional outcomes.

The null hypothesis is that there are improvements in primary outcomes in KA MP TKA compared to MA MP TKA patients. The secondary hypothesis will investigate whether there is a statistically significant difference in HKA and implant position between KA and MA patients in our cohorts and if there are any differences in complication and revision rate between both cohorts.

# 2 Materials and Methods

## 2.1 Design of the study

Results of prospectively collected 24 patients (13 females and 11 males) operated with a non-restricted calipered kinematically aligned technique and a medial pivot implant were compared with the same number of patients and implants under MA principles, both operated with conventional instruments and resection of PCL. Matching was performed by comparing sex, age (within +/-5), HKA axis (+/- 5°), and BMI (+/-5 $Kg/m^2$).

**Table 1: Comparation of demographic data with preoperative PROMs scores and radiological measurements between kinamatically aligned KA TKA and mechanically aligned MA TKA groups. Data shown as mean values (Jeremić et al. 2020). (Author copyrights requested and granted from Elsevier Publishing).**

| | Kinematic Alignment group (n=24) | Mechanical Alignment group (n=24) | p-Value |
|---|---|---|---|
| **Age (years)** | 70.7(6.7) (55 - 80) | 72.5 (5.8) (60 - 85) | 0.32 |
| **Body mass index** | 30.6 (4.5) (23-39) | 30.0 (4) (22-37) | 0.28 |
| **Preoperative HKA** | -4.9 (6.1) (-15 - 10.7) | -5.2 (6) (-17.8 - 11) | 0.54 |
| **Preoperative MPTA** | 85.9 (3.6) (77-92) | 86.8 (3.4) (80-93) | 0.8 |
| **Preoperative LDFA** | 89.2 (2.2) (86-94) | 89.0 (2.7) (83-94) | 0.2 |
| **Preoperative JLCA** | 3.4 (1.9) (0-6,5) | 4.2 (2) (2-11) | 0.19 |
| **Preoperative new Knee Society Score** | | | |
| Objective knee indicators (100) | 35.6 (24.7) (0-78) | 26.8 (20.7) (1-70) | 0.09 |
| Patient satisfaction (40) | 12.1 (5.0) (4-24) | 8.9 (3.3) (4-18) | 0.01 |
| Patient expectations (15) | 14.4 (1.1) (11-15) | 13.8 (1.4) (9-15) | 0.1 |
| Functional activities (100) | 29.4 (12.0) (7-51) | 27.2 (10.0) (3-45) | 0.45 |
| **Preoperative KOOS** | | | |
| symptoms (100) | 41.7 (18.2) (14-75) | 37.1 (11.4) (21-57) | 0.24 |
| pain (100) | 36.0 (13.4) (3-55) | 32.8 (8.9) (19-50) | 0.2 |
| ADL (100) | 37.9 (13.4) (10-66) | 37.9 (13.4) (20-53) | 0.29 |
| Sport (100) | 9.0 (9.8) (0-30) | 9.2 (8.4) (0-25) | 0.87 |
| QOL (100) | 21.9 (11.8) (0-50) | 20.8 (7.7) (6-37) | 0.68 |

Demographics of both groups are illustrated in Table 1 (Jeremić et al. 2020). Matching was done within of 5 degrees of deformity (valgus phenotype or varus phenotype). No restrictive preoperative limb deformity criteria were included. No patients were excluded because of complications suffered in shown period. Traumatic osteoarthritis and previous knee arthrotomy before index surgery were exclusion criteria. The study was registered under No. NCT03446391 after confirmed consent of all participants in both cohorts and approval from University Münster ethical committee (P02.010.18).

## 2.2 Operative technique

Both groups were operated without tourniquet in manual operative technique through a medial parapatellar surgical approach using standard instrumentation and cemented cruciate sacrificing medial stabilized joint replacement GMK Sphere – (Medacta, Switzerland). Calipered unrestricted Howell technique (Howell 2019; Jeremić and Haaker 2020) was used by manually performing KA implantations. The goal was to position the implants to reconstruct the prearthrotic joint line orientation without ligaments release. The resected distal and posterior femoral bone was measured to verify that femoral bone thickness matched implant thickness. The worn cartilage and saw blade thickness were added in measurements where necessary.

Recut guides and use of washers by over-resection on distal femur were used after addressing gaps (in flexion and extension) with spacer blocks as constituent part of KA technique (Howell 2019; Jeremić und Haaker 2020). MA implantation was fashioned by measured resection femur first technique. Femoral side component rotation was referenced to posterior condylar line with 3° external rotation with tibial neutral (90°) resections and tibial slope of 3°. The MA strives to achieve neutral limb alignment and intramedullary femoral and extramedullary tibial alignment guides were used in that matter. Collateral ligaments were released, if necessary according to the ligament balancing technique that is extensively studied in publications (Mihalko et al. 2009). The postoperative protocol was identical for both of groups, and the surgeries were done by surgeon familiar in both techniques. Both groups were performed without any patella resurfacing.

## 2.3 PROMs analysis

Patient related outcome measures (PROMS) were collected in the outpatient department at regular postoperative visits at 6 weeks and 1 year. PROMS included the preoperative and postoperative values of new Knee Society score (KSS) and Knee Injury and Osteoarthritis Outcomes Score (KOOS), as well as postoperative values of Forgotten Joint Score (FJS).

All results in the patient-related outcome measures were self-reported by the patient, excluding the objective section of KSS. Complication and reoperations are recorded for both cohorts.

## 2.4 Radiological analysis

For every patient limb and knee measurements were done with mediCAD Software 1.84 (Hectec Gmbh, Germany) in coronal plane. Assessment of hip knee angle axis (HKA), medial proximal tibial angle (MPTA), lateral distal femur angle (LDFA), and joint line convergence angle (JLCA) were recorded between both groups (Figure 1). All measurements were done pre and postoperatively.

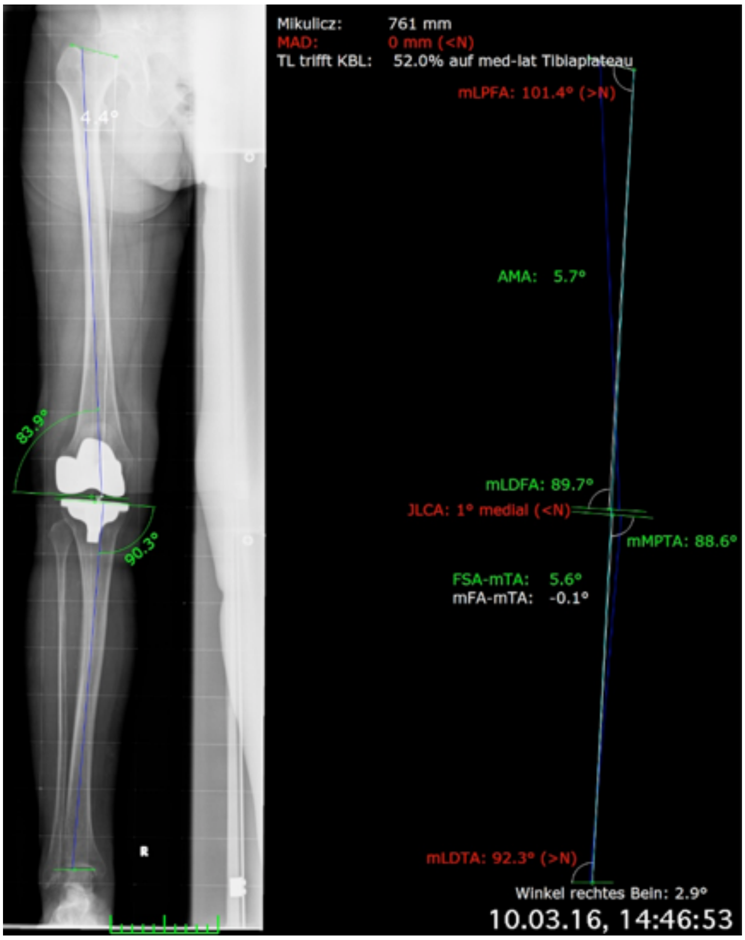


**Figure 1: Postoperative measurements of the coronal alignment (HKA), joint line obliquity (JLCA), and implant positioning (MPTA and DLFA)**

## 2.5 Statistical methods

In order to capture difference of the functional KSS (8 points), which estimated a sample size, each group has to have a minimum of 22 patients, for level of significance $\alpha$ of 0.05 and to be powered with $\beta$ of 80%. Assuming a potential loss of 10% to follow-up at one-year period, per group were included 24 patients.

Normal distribution of demographic data was verified using Shapiro-Wilk test. Paired Student t-test was used for normally distributed continuous data and Wilcoxon signed-rank test for non- normally distribution. Paired categorical group data was verified using McNemar test. Categorical and continuously distributed (normally and non-normally) data are shown as mean value (SD, minimum to maximum), median value (IQ range, minimum to maximum) and percentage.

There was no missing data. Statistical analysis was done with the Minitab and R software. Statistical significance was set at $p < 0.05$. Statistical analysis is similar with data already published in index publication (Jeremić et al. 2020).

# 3 Results

## 3.1 Primary outcomes

Both groups of patients showed statistically significant improvements to preoperative scores. This was systematically presented foremost in the sport section of the KOOS score (Figure 2).

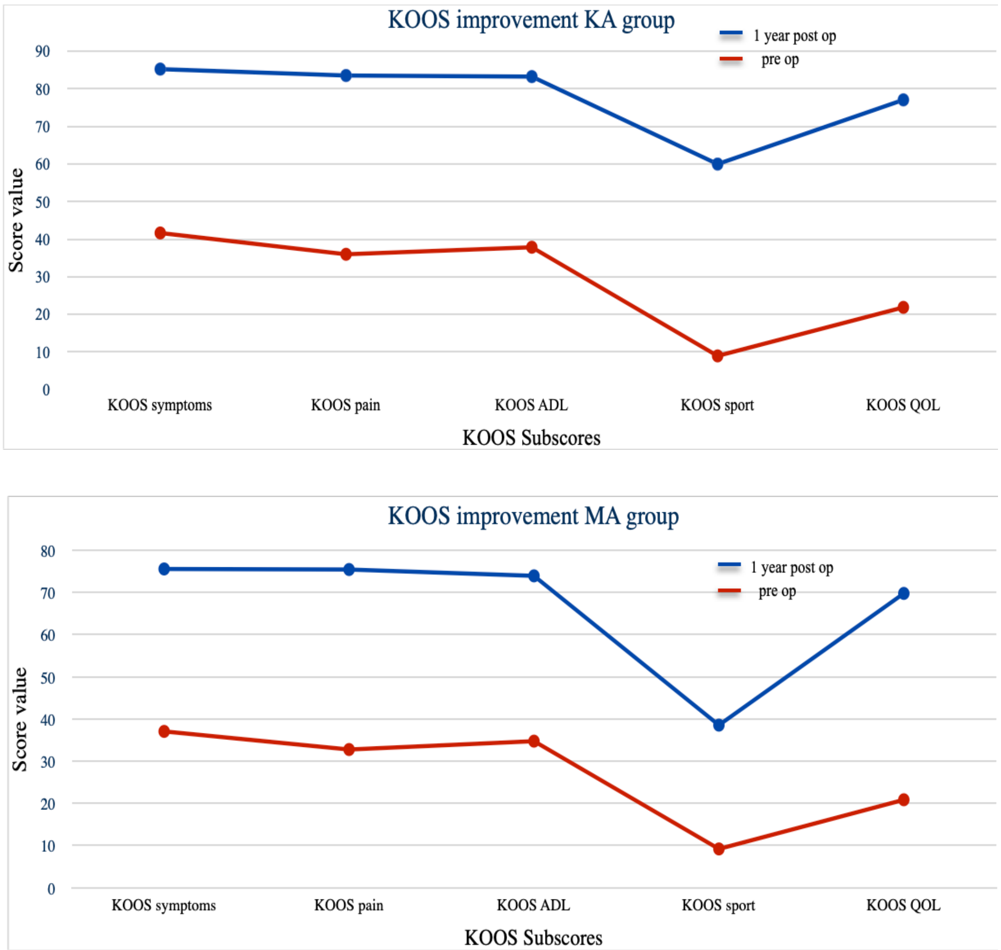


**Figure 2: Preoperative to 1-year improvements in both KA and MA group regarding KOOS score.**

Regarding FJS, at 6-weeks follow-up median values were KA 39 vs MA 23 ($p = 0.02$). Similarly at 1-year follow-up medial values of FJS showed KA 77 vs MA 51; ($p = 0.05$) (Figure 3, Table 3).

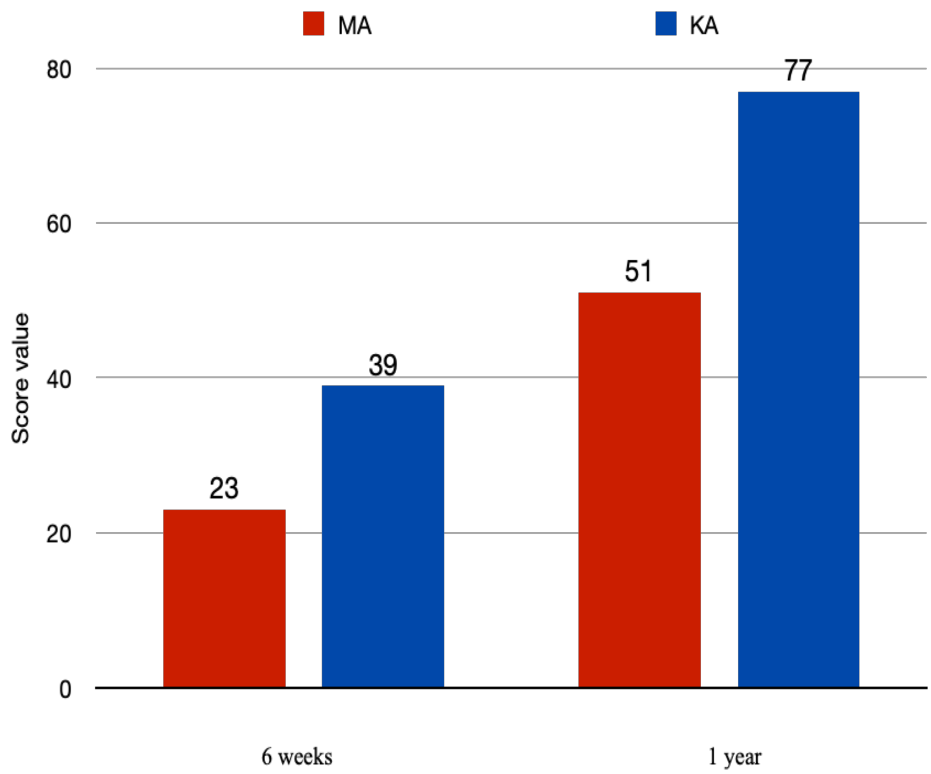


**Figure 3: Comparation median values of Forgotten joint score (FJS) between kinamatically aligned and mechnically aligned groups in 6 weeks and 1 year**

When considering mean values of FJS, in follow-ups at 6 weeks kinematically aligned group performed better than mechanically aligned (39 (17) compared to 26 (10); $p < 0.01$) respectively, as well as at 1 year (kinematically aligned group 71.5 (29) compared to mechanically aligned group 51 (20); $p = 0.05$). (Table 2). The sport section of KOOS showed statistically significant difference between groups in favor of KA (Table 2).

In the new KSS score, KA group of patients outscored MA group of patients solely for the objective knee indicators (Table 3, Figure 4).

**Table 2: Functional outcomes of FJS, KOOS and new KSS after 6-weeks shown as mean values between kinematically and mechanically aligned group**

| | KA group | MA group | p-value |
|---|---|---|---|
| **FJS** | 39.1 (17.0) | 26.1 (17.0) | 0.02 |
| **new KSS** | | | |
| • Objective knee indicators (100) | 74.2 (17.3) | 59.6(14.7) | 0.01 |
| • Patient satisfaction (40) | 25.7 (6.1) | 24.3 (4.2) | 0.44 |
| • Patient expectations (15) | 10.1 (2) | 10.3 (2) | 0.53 |
| • Functional activities (100) | 31.7 (13.3) | 35.5 (12.3) | 0.31 |
| **KOOS** | | | |
| • symptoms (100) | 58.5 (17.2) | 56.5 (9.0) | 0.67 |
| • pain (100) | 48.5 (17.5) | 53.5 (7.6) | 0.26 |
| • ADL (100) | 55.6 (18.1) | 49.8 (8.0) | 0.22 |
| • Sport (100) | 20.8 (21.1) | 9.8 (11.2) | 0.01 |
| • QOL (100) | 36.5 (23.7) | 45.6 (12.2) | 0.12 |

**Table 3: Functional outcomes of FJS, KOOS and new KSS after 1-year shown as mean values between kinematically and mechanically aligned group (Jeremić et al. 2020). (Author copyrights requested and granted from Elsevier Publishing).**

| | **KA group** | **MA group** | **p-value** |
|---|---|---|---|
| **FJS** | 71.5 (28.5) | 51.2 (19.6) | 0.05 |
| **new KSS** | | | |
| • Objective knee indicators (100) | 86.0 (17.9) | 71.5(16.8) | 0.02 |
| • Patient satisfaction (40) | 33.2 (8.5) | 29.4 (8.0) | 0.08 |
| • Patient expectations (15) | 9.9 (2.9) | 9.9 (2.9) | 0.7 |
| • Functional activities (100) | 64.3 (13.4) | 57.1 (14.3) | 0.09 |
| **KOOS** | | | |
| • symptoms (100) | 85.3 (14.2) | 75.6 (15.6) | 0.07 |
| • pain (100) | 83.6 (16.3) | 75.5 (16.2) | 0.18 |
| • ADL (100) | 83.3 (15.0) | 74.0 (14.6) | 0.1 |
| • Sport (100) | 60.0 (24.5) | 38.5 (20.4) | 0.01 |
| • QOL (100) | 77.1 (22.4) | 69.8 (18.9) | 0.26 |

**Table 4: Functional outcomes of FJS, KOOS and new KSS after 1-year shown as median values between kinematically and mechanically aligned groups (Jeremić et al. 2020). (Author copyrights requested and granted from Elsevier)**

| | KA group | MA group | p-Value |
|---|---|---|---|
| **FJS** | 77 (58-96) (0-100) | 51(39-67) (12-89) | 0.05 |
| **New KSS** | | | |
| • Objective knee indicators (100) | 94.0(79-98) (41-100) | 75.0(61-82) (30-95) | 0.02 |
| • Patient satisfaction (40) | 36.0(32-38) (6-40) | 30.0(22-30) (12-40) | 0.08 |
| • Patient expectations (15) | 9.0(9-11) (3-15) | 9.0(7-10) (6-15) | 0.70 |
| • Functional activities (100) | 67.0(54-74) (23-80) | 60.0(46-69) (25-82) | 0.09 |
| KOOS | | | |
| • symptoms (100) | 89.3(72-96) (50-100) | 78.5(64-88) (42-100) | 0.07 |
| • pain (100) | 84.7(75-99) (42-100) | 72.2(61-91) (39-97) | 0.18 |
| • ADL (100) | 88.2(73-94) (46-100) | 73.5(64-84) (37-96) | 0.10 |
| • Sport (100) | 65.0(45-75) (10-95) | 40.0(20-55) (0-75) | 0.01 |
| • QOL (100) | 81.2(68-93) (6-100) | 71.8(20-55) (37,5-94) | 0.26 |

Regarding delta values (pre- and 1-year post-op results) KA group of patients had statistically significant differences in improvement just in s port section of the KOOS (Table 5).

**Table 5: Improvements preoperatively to 1 year in KOOS and new KSS between kinematically and mechanically aligned groups. Results are expressed as mean (standard deviation) (Jeremić et al. 2020) (Author copyrights requested and granted from Elsevier).**

| | KA group | MA group | Difference between groups | p-Value |
|---|---|---|---|---|
| **New KSS** | | | | |
| • Objective knee indicators (100) | 50.3 (34.2) | 44.7(25.7) | +5.6 (8.5) | 0.5 |
| • Patient satisfaction (40) | 21.1 (9.3) | 20.5 (8.8) | +1.5 (0.5) | 0.83 |
| • Patient expectations (15) | 4.5 (3.4) | 4.2 (3.5) | +0.2 (0.1) | 0.98 |
| • Functional activities (100) | 34.8(16.7) | 29.9(16) | +4.9 (0.7) | 0.33 |
| **KOOS** | | | | |
| • symptoms (100) | 43.6 (20.5) | 38.5 (17.8) | +5.1 (2.6) | 0.43 |
| • pain (100) | 47.6 (22.1) | 42.7 (17.1) | +4.9 (5.0) | 0.49 |
| • ADL (100) | 45.4 (19.4) | 39.2 (15.9) | +6.2 (3.4) | 0.31 |
| • Sport (100) | 51.0 (24.5) | 29.4 (21.5) | +21.7 (3) | 0.01 |
| • QOL (100) | 55.2 (23.9) | 49.0 (18.8) | +6.22 (5.2) | 0.35 |

## 3.2 Secondary outcomes

Preoperative values between the KA and MA groups are illustrated In Table 1. Preoperative standing hip-knee-ankle axis showed no statistical difference between groups (p = 0.54). The p-value between both groups were: (p = 0.54) for the medial proximal tibial angle (MPTA), (p = 0.8) for he distal lateral femoral angle (DLFA), and (p = 0.19) for the joint line convergence angle (JLCA) (Table 1).

Postoperatively, the mean HKA and varus/valgus angles of orientation of implant components were similar between the two groups in frontal plane (Table 5). Within KA patients group, 11 (46%) and within MA patients group 7 (29%) had a more than 3° deviation from neutral (180°) alignment (p = 0.388). The medial tibial proximal angle was postoperatively more than 87° in 70% of KA patients, compared to 58% in MA group ($p = 0.62$).

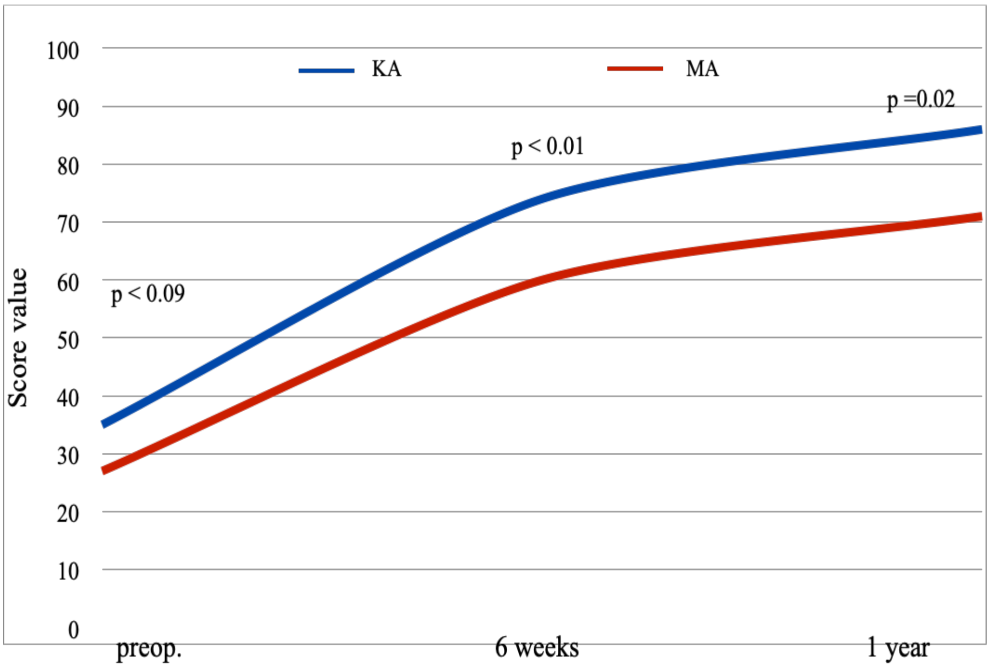


**Figure 4: Comparation of postoperative objective knee indicators of Knee Society Score (KSS) between kinematically and mechanically aligned groups in 6 weeks and 1 year and a statistically significant difference between both techniques.**

**Table 6: Comparation of postoperative coronal alignment between KA TKA and MA TKA groups. Data shown as hip-knee-ankle, lateral distal femoral, medial proximal tibial and joint line convergence angles (Jeremić et al. 2020) (Author copyrights requested and granted from Elsevier).**

| | KA group | MA group | p-value |
|---|---|---|---|
| HKA | -0.2(3.6) (-9°to7.4°) | -0.3(2.7) (-4.1 5°) | 0.97 |
| MPTA | 88.4° (2.1) (83°to 92°) | 89.0(2.1) (83°to 90°) | 0.5 |
| LDFA | 88.5° (3.5) (83°to 95°) | 89.9(2.8) (83°to 92°) | 0.08 |
| JLCA | 0.5 (0.8) (0°to 4.2°) | 0.9(1.5) (0°to 6.3) | 0.07 |

In both groups in the 1-year follow-up, there were no complications and no revision surgeries recorded.

# 4 Discussion

This study illustrates how the KA patients had better outcome scores in FJS at 6 weeks and 1-year follow-up compared with MA patients. Similar findings were demonstrated for the sport section of KOOS and objective score of KSS. There were also superior outcome scores in the KOOS and new KSS scores for the KA group; however, these outcomes were not statistically different. Overall, there were improvements in both cohorts regarding their preoperative values.

## 4.1 Primary outcomes

Analysis of the results at 6 weeks and one year, demonstrates statistically significant results that demonstrated better outcome in FJS for the KA group and minimal differences in the objective score KSS and sports section KOOS, when compared with the MA group.

The early postoperative results of 6 weeks expressed as KSS mean in this study were comparable with data reported by Waterson (2016) in his RCT showed 65.7 (13.1) in KA group versus 59.0 (9.2) in MA group ($p = 0.05$), underlining results from this study favoring KA to MA group 74.2 (17.3) versus 59.6 (14.7), respectively. Furthermore, Waterson study showed no statistically significant difference between both groups expressed as KSS mean in 3 months follow-up with results KA 78.4 (21.1) vs 69.1(17.5) ($p = 0.09$). These trend stays further as 6 months and 1 year follow-up with ($p = 0.62$) and ($p = 0.42$) respectively. In the same study 6 weeks outcome measures of KOOS were comparable between both groups 59.0 (15.0) comparing to 59.0 (15.7) ($p=0.99$), and in accordance with 6 weeks results of these study where KA group performed without statistical difference to MA group 58.5 (17.2) to 56.5 (9.0) ($p = 0.67$).

By contrast study of Elbuluk (2022) comparing 6 weeks KOOS mean values reported favoring results in a kinematically aligned group 71.0 (3) to mechanically aligned 60.0 (4) ($p < 0.05$). These differences could be partially driven with patient selection in Elbuluk study, which included only varus knees deformity and is done with robotic assisted surgery, underlining mechanical alignment deficiencies comparing to navigation and manual performance of mechanical alignment in Waterson and here presented study. In the same study of Elbuluk et al., 6 weeks FJS postoperative results showed no differences between groups, reporting 57.2 (8.9) and 53.4 (6.4) ($p = 0.9$) for KA and MA, respectively. This contrasted results from this thesis with postoperative 6 weeks FJS at 39.1 (17.0) in kinematically aligned and 26.1 (10.39) in mechanically aligned group showing statistically difference ($p < 0.03$) favoring KA group. Overall FJS 6 weeks results were lower in matched paired study suggesting that significant demographic differences between urban USA population patients vs rural German population could play a role in underscoring in this study. But in general differences suggesting superior KA results is to be drawn in a patient selection which didn´t excluded any deformities and was done without ligament releases, thus supporting early outcomes in KA group.

KA performance in this study is comparable with results reported by (French et al. 2020). RCT results of KA MP TKA showed FJS mean of 79.9 (20.4) after one-year follow-up which is similar to the mean of 71.1 (28.5) from this study. This study illustrates the combination of MP and KA as a possible synergistic concept that favor both knee kinematics and preserving the soft tissue envelope. In a different study, Young et al.(2017) found similar FJS in their randomized trial having compared 49 KA to 50 MA patients at 2 years follow-up, both groups had very high FJS. The mean was 69 for the KA group and 66 for the MA group. One possible explanation to these findings may be the use of imprecise personalized instrumentation for the KA group in addition with inadequate use of collateral release, both of which are not part of the technique (MacDessi et al. 2020). This study’s FJS mean of 71 (28.5) in the KA group is similar to KA results published in the Young study.

On the other hand, 1 year outcomes FJS of KA to MA group in this thesis, 71.5 (28.5) and 51.2 (19.6), ($p < 0.03$), were superior than outcome measure of RCT FJS in study of MacDessi et al. (2020) which with 63.9 (26.6) and 56.8 (26.0) ($p = 0.15$), respectively for KA and MA alignments. That MA results showed similar functional outcome KA results in our group is to be partially explained with restrictive alignment targets and bounding restrictive patient selection regarding safe-zones in femoral and tibial coronal alignment in MacDessi study. It was reported in almost 31% of patients in kinematically aligned group isolated soft tissue release with or without bone recuts, what is in contrary to this work where no releases in KA group were done, excluding bone recuts which are inevitable in unrestricted KA technique as bone adjustment is how changes in soft tissue tension is done. Furthermore, number of releases in MacDessi study is very similar between both MA and KA groups, 11 (16%) vs 16 (23%), respectively.

The FJS results from the current research are comparable to the average values of FJS in general population for the USA. These values are established to enhance the interpretability of FJS and are presented as mean and median values (Giesinger et al. 2019). In this study in a population older than 70 years of age, the FJS mean values were 73 (+/- 30.5). Among KA patients FJS values expressed as, mean, SD, and median of 71.3 (+/- 28.4) and median of 77 were similar to standardized values in the work of Giesinger compared to the MA TKA group's values of 51.2 (+/-19.6) and median 51.

In their mid-term follow-up comparing patients with two staged KA/MA TKA, (Shelton et al. 2019a) found FJS to have median FJS 75 for the KA group and median FJS 60 in the MA group, which is in keeping with the median FJS of 77 for the KA group and 51 for the MA patients in this study. (McEwen et al. 2019) in their bilateral KA/MA RCT study demonstrated that a significant proportion of patients preferred the KA operated side but have reported FJS of 79.9 (23.5) in the KA group, also with a high FJS in the MA group 79.6 (19.4). These results are much higher than the mean of 71.3 (28.4) in the KA group to 51 (19.6) in the MA group from this study. These outcomes suggest that the functional ability and recovery of the KA group is superior to the MA group.

Recently published study of Ebuluk (2022) comparation to robotic assisted KA vs MA TKA, where the results of FJS from 1 year and 2 year results of 88 +/- 6,9 for KA group vs 72,4 +/- 5,8 for MA group ($p < 0.001$) and 88 +/- 6,9 for KA group vs 72,4 +/- 5,8 for MA group ($p < 0.001$) , respectively are similar to 1 year results of FJS from this study. This can be considered complementary to the above-mentioned studies. Contrary the 6 weeks FJS gave no differences between both groups KA vs MA, which suggest that the possible differences in demographics and preoperative scores may play a role.

Study from Vignorchik (2022) showed that in group without ligament releases which addressed just bone recuts (Jeremić und Haaker 2020) the better PROMS outcomes are to be reported in 6 week and 2 year group respectively. Which are in accordance with results of this thesis with regard of no releases in KA TKA group, and speaks to very concept of KA TKA without ligament releases and exclusively bone recuts as way to achieve soft tissue tension of the joint.

Regarding the improvements of pre- to postoperative KSS and KOOS, only MacDessi (2020) RCT study reported patient reported outcome measures between KA and MA groups. Both groups were operated with intraoperative navigation and pressure sensor insert and follow up was set to 1 year. These results are complementary with outcomes from this study which reported no statistically significant difference but sports section of KSS which favors KA ($p < 0.01$), and trend toward statistically difference in MacDessi study ($p = 0.08$).

Due to the nature of protocols applied to the tibial cut in KA, there are only a few studies that can be compared to outcomes of KSS and KOOS from this work. The study by (Matsumoto et al. 2017) demonstrated statistically significant differences in the KSS scores in both the objective and functional parts. The results from this study complement these outcomes in objective outcomes. Another study, from (Blakeney et al. 2019), assessed KOOS as a combined secondary outcome and showed a statistically significant difference with higher scores in the KA group compared to the MA group (74 vs. 61, $p = 0.034$). Comparable results with KOOS combined 77.84 in KA to 66.67 in MA group ($p = 0.06$) are shown in this thesis. This supports better outcome scores in KA group with less ligament balancing and more physiological soft tissues tension. In another study, (MacDessi et al. 2020) showed no difference in KOOS sub scores. This may be attributed to the use of one specific implant. The results of this study are partially in accordance with the findings by (Waterson et al. 2016) RCT, who compared 35 conventional MA to 36 PSI KA and reported statistical differences in KOOS scores after 6 weeks, but no difference between KA and MA when they reached ceiling effect after 1 year.

Kinematic alignment was proved to be effective in short term outcomes, and probably better than MA counterparts. Recent publication compared MA TKA and KA TKA done with similar cruciate retaining fixed bearing implant and with robotic assisted intraoperative tool. They find statistically significant difference in 6 weeks KA group 71 (4) vs MA group 60 (3) ($p<0.05$) , in 1 year KA group 88 (6) vs MA group 73(5) ($p<0.05$) and 2 year KA 94 (5) vs. MA 84 (4) ($p<0.05$) in KOOS (Elbuluk et al. 2022). These results are comparable with results from present study with 6 weeks KOOS values of 58 (17 ) in KA and 56 (9 ) in MA group (p=0,26), at one year postoperative scores were comparable with above mentioned study with results ranging for 85 (15) in KA group vs 75 (14) in MA group ($p = 0.08$). Those results are in line with previous studies and RCT of Dosset et al (2012) and Callies et al (2017).

Blakeney (2019) compared the KOOS between KA (with restricted protocol) and MA TKAs. Blakneys KA group was operated either as KA TKA or restricted KATKA, and this results cannot therefore be compared to from this thesis. It is probable that the absence of statistical significance in KOOS comparison be partly explained by a statistical error type II (lack of power of our statistical tests) and the low sensitivity of the KOOS (high ceiling effect) (Thomsen et al. 2016). The interpretation of the overall better 'new KSS' and KOOS scores found for our KA patients remain elusive: it may be the result of a true functional superiority of physiological KATKA implantation over non-physiological MATKA ones, but it may have also been favored in the KA group with better pre-operative KOOS and KSS.

## 4.2 Secondary outcomes

Similar radiological outcomes were found in both techniques. Overall alignment showed no significant differences, which is in keeping with previous studies. This may be due to a smaller sample size that could results in a Type II error. The intragroup comparative power is caused by deviations of desired alignment in the MA group and can be also potentially be explained by the correlation with specific knee phenotypes in our population (Hess et al. 2019; Hirschmann et al. 2019).

In this study, the HKA axis of 46% of patients in the KA group were outside of +/-3° compared with 28% in the MA group.

In 17 of the 24 (70%) patients in the KA group, MPTA was over 87° in relation to 14 (58%) patients in the MA group (Almaawi et al. 2017). Our data regarding postoperative LDFA and MPTA are not in line with previous RCTs studies ((Dossett et al. 2014; Calliess et al. 2017; Matsumoto et al. 2017; Young et al. 2017) Comparing the results of this study with RCTs, we had varus 1.6°((2), (-6°- 2°)) in tibial component relative to anatomical axis of tibia in KA group, which is in contrast to varus 2°((2.2),( -8.7°-4°) found in Dossett et al. (2014) study, as well as 2° (1) in Calliess et al. (2017). On the other hand, Waterson et al. (2016) had 3° (-10° - 3°) and Young et al. (2017) reported MPTA with 3° varus (3), (-10°-4°). Our results showed that in underpowered analysis DLFA of $p < 0.08$ and JLCA $p < 0.07$ could be a compensatory factor for better results in KA group.

Their results could be affected by a too small sample size, but also by imprecision in 2D measurements. That this is the only study that compared manually done KA vs. manually operated MA.

Overall alignment was within range for both groups. The limb and knee alignment in KA TKA was similar to those of MA TKA, while the component alignment showed no statistical differences (p = 0.49) in the tibial component and mild valgus in the femoral component in KA TKA (less 0.08). Our results are in contrast to published studies that also found varus of greater than 2 degrees. (Dossett et al. 2014; Hutt et al. 2016; Matsumoto et al. 2017; Niki et al. 2018). It is evident from this study that rotational, sagittal, and dynamic alignment plays a greater role in outcomes of KA in addition to coronal alignment.

There were no reoperations or revisions in any groups. This is in accordance with combined Australian and New Zealand registry data , which showed cumulative rate of revisions for any cause for KA groups to be 3,1% and for all other alignment groups 3,0 % (Klasan et al. 2020).

This study has some limitations. Implant desired alignment measured with MPTA and DLFA showed deviations that may have affected the outcome. It is possible that a Type II error could have occurred if the mechanically aligned group did not vary significantly in implant positioning alignment in comparison with the KA group. It may have been impeded by the two-dimensional nature of the measurements and small sample. More imposed restriction of matching criteria, consideration of more parameters, and randomization would potentially impact results. The difference between matching groups in preoperative satisfaction most probably had marginal influence on the results, although they are in concordance with validated peer review publications (Dossett et al. 2014; Almaawi et al. 2017; Calliess et al.2017; Matsumoto et al. 2017; Blakeney et al. 2019; Shelton et al. 2019).

Secondly, a longer follow up period that could influence differences between groups, complication reporting, and implant survivorship could favor to the results of the thesis.

# 5 Conclusion

This work investigated functional and radiological outcome, with primary results of PROMs, secondary trough HKA alignment and complication rate after KA TKA and MA TKA based on results of multiple studies. KA TKA group reported better PROMs (FJS, some aspects of KOOS and KSS) than group after MA TKA. Deformity restrictions in selection of patients for KA cohort could bias the results favoring mechanically aligned TKA. Radiologically, no difference between both techniques in the limb alignment and HKA angle could be found. The 3D accuracy and reconstruction of oblique joint line and slope of kinematic alignment underscores the difference between both alignments and may be explanation of superior outcomes in kinematically aligned group of patients. The precision of intraoperative assistive tools (robotics, PSI, navigation) was put in question by deviation of tibial resection in up to 40 % of cases, by 1 mm over- and under resection (Howell et al. 2022). Unrestricted caliper verified kinematic alignment with 0,5 mm deviations overperform intraoperative assistive tools with its accuracy.

The design of medial stabilized TKA combined with kinematic alignment could be a favoring option for reconstruction of prearthritic alignment, restoring joint line obliquity and addressing advances of kinematics of TKA. A combination of both concepts provides a better functional Forgotten Joint Score, which ultimately leads to greater satisfaction in TKA patients. Further research in differentiation between both concepts and how new technologies and more sensitive scores could potentially underline clinical difference between alignment techniques is necessary.

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# CV

Dr Jeremic native of Belgrade works as a consultant orthopedic surgeon in St.Vinsenz Hospital Arthroplasty Center in Brakel, specializing in knee and hip arthroplasty.

Dr Jeremic did his graduate studies in Belgrade at local Medical University, afterwards interest in skeletal surgery brought him to Germany where he finished residency in 2009 and did board exam at Low Saxony Medical Chamber. His further education continued at University of Aachen and Bruderkrankenhaus Paderborn. From 2011 onwards he is attending physician at Arhtroplasty Center Brakel. In 2016 he was fellowship trained in Northwestern Memorial Hospital, Northwestern University, Chicago. In 2017 he got subspecialisation in special orthopedic surgery by Westphalia-Lippe Chamber of Medicine where he is member. He is senior surgeon in arthroplasty Center and his operative volume is around 350 joint replacement a year.

He has been one of the first adopters of the kinematic alignment technique (contributed to Dr Stephen Howell) and is preforming this technique for the last 8 years.

He is a well-recognized pioneer for the instrumented non-restricted kinematic alignment technique in Europe. Generating a fast-growing practice and extensive proctoring programs for surgeons from all over Europe for the emerging kinematic alignment technique concept, Dr Jeremic holds position as part of the international advisory group for kinematic alignment.

His current research project focus on the clinical outcome comparison of kinematic and mechanical alignment as well as radiological analysis.