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Lower limb phenotypes - the future of total knee arthroplasty: a systematic review

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Junho de 2023

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DECLARAÇÃO DE INTEGRIDADE

Declaro ter atuado com integridade na elaboração da presente tese. Confirmo que em todo o trabalho conducente à sua elaboração não recorri à prática de plágio ou a qualquer forma de falsificação de resultados.

(Fabiana Santos)

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Coorientador:

(Dr. Pedro Cardoso)

Junho de 2023

Resumo

Introdução e objetivos: Ao longo de décadas, a artroplastia total do joelho tem aplicado o alinhamento mecânico - uma abordagem sistemática que resulta num membro inferior alinhado de forma neutra. Embora as próteses do joelho alinhadas de acordo com este racional mostrem uma boa durabilidade a longo prazo, os seus resultados funcionais têm-se mostrado, por vezes, subótimos. Estes desfechos insatisfatórios persistem apesar dos avanços nos *designs* de próteses e em tecnologias de auxílio à implantação, o que sugere que o problema possa estar inerente à técnica de alinhamento mecânico em si. Têm vindo a ser propostas alternativas de alinhamento para prótese do joelho, sendo o alinhamento cinemático o mais estudado. O alinhamento cinemático apresenta como objetivo o restauro do alinhamento individual de cada doente, sob o racional de que replicar da anatomia, cinemática e equilíbrio dos tecidos moles irá melhorar os resultados funcionais da prótese total do joelho. No entanto, alguns autores têm mostrado reticências quanto à aplicação deste método em doentes com deformidades mais extremas, uma vez que podem não ser compatíveis com as próteses e métodos de fixação atuais e por isso resultar em complicações e/ou numa menor durabilidade da prótese do joelho. Esta revisão sistemática pretende responder à seguinte questão: as formas alternativas de alinhamento melhoram os resultados funcionais da prótese total do joelho, quando comparadas ao alinhamento mecânico? Outros dados analisados incluem o equilíbrio ligamentar, o alinhamento pós-operatório e a taxa de complicações.

Métodos: Foi realizada uma revisão sistemática da literatura em dezembro de 2022, utilizando as bases de dados PubMed e Google Scholar. Foram incluídos apenas estudos retrospetivos, prospetivos e ensaios clínicos randomizados publicados nos últimos 15 anos (dezembro 2007 – dezembro 2022) em inglês, francês ou português. Entre os 847 artigos identificados, 10 estudos preencheram os nossos critérios de inclusão. As características e conclusões relevantes de cada estudo foram sintetizadas numa tabela. Foi aplicada a ferramenta da Cochrane para uma avaliação formal do risco de viés dos artigos incluídos.

Resultados: Não foram encontradas diferenças estatisticamente significativas nos resultados funcionais aos 5 anos das próteses totais do joelho implantadas com o alinhamento cinemático, em comparação com o alinhamento mecânico. Em termos de equilíbrio ligamentar, o alinhamento cinemático foi vantajoso em relação ao alinhamento mecânico. O alinhamento coronal do membro inferior foi semelhante em ambos os grupos, embora o componente tibial tendesse a estar ligeiramente mais varo no grupo de alinhamento cinemático, e o componente femoral mais valgo. As taxas de complicações a curto prazo e de revisão cirúrgica foram semelhantes entre as artroplastias totais do joelho realizadas com alinhamento cinemático e alinhamento mecânico em todos os estudos, e a sobrevida aos 5 anos livre de reoperação/revisão (modelo Kaplan-Meier) também foi idêntica.

Discussão: A avaliação do risco de viés levantou algumas questões quanto à validade interna dos estudos incluídos. A impossibilidade de ocultar os cirurgiões da intervenção e a experiência distinta com as diferentes opções de alinhamento são algumas das limitações encontradas. Além disso, alguns estudos introduziram variáveis de confundimento ao utilizarem diferentes técnicas cirúrgicas entre grupos. A validade externa de alguns estudos também se revelou questionável, uma vez que excluíram doentes com deformidade em valgo ou deformidades mais severas. Além disso, o estudo com maior duração incluído nesta revisão realizou um seguimento de 5 anos, período insuficiente para avaliar possíveis complicações a longo prazo e a durabilidade da prótese.

Conclusão: Não encontrámos diferenças entre as próteses de joelho aplicadas com o alinhamento cinemático ou mecânico no que diz respeito aos resultados funcionais aos 5 anos. Atualmente, o alinhamento cinemático implica modificações no alinhamento dos componentes femoral/tibial que têm um impacto desconhecido na longevidade da prótese do joelho e complicações a longo prazo. Para melhor compreender os efeitos a longo prazo de uma prótese alinhada segundo o método cinemático, são necessários estudos com uma seleção mais abrangente de doentes e com períodos de seguimento mais alongados. Até lá, e dada a ausência de benefícios funcionais óbvios do alinhamento cinemático, a aplicação deste tipo de alinhamento deve ser feita com cautela.

Palavras-chave: Articulação do Joelho / anomalia, anatomia e histologia, fisiologia, cirurgia; Prótese do Joelho; Artroplastia, Substituição, Joelho / instrumentação, métodos; Fenómenos Biomecânicos.

Abstract

Background and objectives: For decades, total knee arthroplasty (TKA) has been performed employing mechanical alignment (MA) – a systematic approach that results in a neutrally aligned lower limb. While MA-TKAs have shown good long-term implant survival, their functional outcomes have been disappointing. Despite advancements in technology and implant designs, these limitations persist, suggesting inherent technical constraints in the MA technique. Alternative alignment options have been proposed, with kinematic alignment being the most studied one. Kinematic alignment aims to restore individual patient-specific alignment, intending to improve clinical results by replicating knee anatomy, kinematics, and soft-tissue balance. However, some authors became concerned about restoring severe pathoanatomies, which may not be compatible with current TKA prostheses and fixation methods, potentially leading to complications and shorter implant survival. This systematic review aims at answering the following question: do alternative alignment options improve functional outcomes of TKA when compared to mechanical alignment? Additional outcomes monitored include knee balance, postoperative alignment, and the rate of complications of TKA.

Methods: A comprehensive systematic review of the literature was conducted in December 2022, using PubMed and Google Scholar as search engines. Only retrospective, prospective, and randomized clinical trials published over the last 15 years (December 2007 – December 2022) in English, French or Portuguese were included. Among 847 reports identified, 10 studies met the eligibility criteria. Study characteristics and extracted data were summarized in tables, and a formal risk of bias assessment was performed using the Cochrane risk of bias tool.

Results: We found no difference in 5-year functional outcomes in TKAs implanted using the KA compared with the MA technique. When evaluating knee balance, kinematic alignment demonstrated an advantage over mechanical alignment. The coronal limb alignment was similar between KA and MA groups, although the tibial component tended to be slightly more varus in the KA group, while the femoral component tended to be more valgus. The short-term complications and surgical revision rates were similar between KA and MA-TKAs in all studies, and the 5-year Kaplan-Meier survivorship free from reoperation/revision was also comparable.

Discussion: The risk of bias assessment revealed some concerns regarding the internal validity of the included studies. The inability to blind surgeons and the variability in their experience with different alignment options were major factors contributing to these concerns. Additionally, some studies introduced confounding variables by utilizing different surgical techniques across groups. In some studies, excluding patients with valgus deformity and severe pathoanatomies may also limit the external validity. Furthermore, the longest follow-up period included in this review was 5 years, which is insufficient to accurately evaluate long-term complications and implant survival.

Conclusion: We found no difference in 5-year functional outcomes in TKAs implanted using the KA compared with the MA technique. Currently, the impact of component alignment variations associated with KA on the longevity of TKA implants and long-term complications remains uncertain. To achieve a more comprehensive understanding of the long-term effects of this alternative approach, it is crucial to conduct further trials that encompass a broader selection of patients and employ extended follow-up periods. Given the absence of definitive functional benefits with KA, caution should be exercised in its utilization until its long-term impact on implant durability is better understood.

Keywords: Knee Joint / abnormalities, anatomy and histology, physiology, surgery; Knee Prosthesis; Arthroplasty, Replacement, Knee / instrumentation, methods; Biomechanical Phenomena

List of abbreviations

AA – anatomic alignment

aMA – adjusted mechanical alignment

CPAK – coronal plane alignment of the knee

EQ-5D-5L – European Quality of Life Measure - 5-Domain - 5-Level

FA – functional alignment alignment

FJS – Forgotten Joint Score

HKA – hip-knee-ankle

ICPD – intercompartmental pressure difference

KA – kinematic alignment

KOOS – Knee Injury and Osteoarthritis Outcome Score

KSS – Knee Society Score

LDFA – lateral distal femoral angle

MA – mechanical alignment

MPTA – medial proximal tibial angle

NR – non reported

OA – osteoarthritis

OKS – Oxford Knee Score (OKS)

ORIF - Open reduction and internal fixation

PROMs – patient-reported outcome measures

RCT – randomized controlled trial

rKA – restricted kinematic alignment

ROM – range of motion

TKA – total knee arthroplasty

WOMAC – The Western Ontario and McMaster Universities Osteoarthritis Index

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Introduction

According to data from the Global Burden of Disease study 2019, osteoarthritis (OA) is still globally prevalent and is expected to increase due to rising obesity and the aging of populations [1]. According to research published in *Arthritis & Rheumatology* “OA in large joints, such as the knee and the hip, causes the most severe disability, and end-stage disease may require joint replacement if available, thus indicating that OA in large joints should comprise a significant proportion of the disease burden” [1]. Total knee arthroplasty (TKA) offers a viable treatment choice for individuals experiencing knee pain caused by osteoarthritis, particularly when conservative treatment approaches have proven ineffective. It is a reliable procedure that provides pain relief and improves the patient’s functional status [2].

Around fifty years ago, Michael Freeman introduced the idea of using right-angled cuts in the femur and tibia during total knee arthroplasty, which led to the emergence of mechanical alignment (MA) [3]. Soon after, John Insall highlighted the importance of balancing the resulting medial-lateral and flexion-extension joint gaps [4]. The mechanical alignment technique subsequently became the standard approach in total knee arthroplasty. This technique is considered "systematic" because it involves implanting all patients in a standardized manner, without considering their individual knee anatomy and soft tissue laxities. This method of implantation was believed to be biomechanically friendly, with the aim of reducing the knee adduction moment and minimizing the risk of an unbalanced prosthetic joint load.

Mechanical alignment total knee arthroplasty (MA-TKA) provides good long-term implant survivorship [5], but its functional outcomes are disappointing, particularly compared to those of total hip replacement [6, 7]. Reports indicate that around 15% of patients who undergo MA-TKA are dissatisfied with the results, while approximately 50% experience residual symptoms such as pain, stiffness, and instability [8]. Despite attempts to improve precision through technology and new implant designs, these issues persist [6], suggesting that there are inherent technical limitations associated with the MA technique. Furthermore, recent research has cast doubt on the reasoning behind the MA technique. For instance: we now know that the standing frontal limb alignment after surgery is not a reliable predictor of prosthetic failure risk [9] or knee compartment load [10]. Additionally, advancements in knee biomechanics have revealed that MA does not fully restore normal alignment of the lower limb and may alter the natural movement of the knee. Some scholars [11] have discovered that the kinetic properties of a healthy knee are governed by three axes: the transverse axis of the femur, the patellar transverse axis, and the longitudinal axis of the tibia. The overall mechanical alignment only considers the two-dimensional alignment of the components with the center of the femoral head, knee, and ankle.

In contrast, the concept of kinematic alignment (KA) diverges from mechanical alignment (MA) by primarily considering the three-dimensional alignment of the components relative to the knee, rather than merely aiming for a neutral hip-knee-ankle (HKA) angle. Based on this concept, Howell et al. [12] introduced kinematic alignment in total knee arthroplasty (KA-TKA) in 2006: "a new custom-fit technique designed to restore the natural prearthritic alignment of the limb and normal kinematics through the use of custom-made tibial and femoral cutting guides constructed from a 3D model of the arthritic knee". This personalized approach to TKA implantation is intended to create a more physiological prosthetic knee and address the aforementioned challenges associated with MA-TKA.

This renewed interest in alternative surgical techniques has led to the development of several alignment options. Currently, there are five alternative techniques challenging the conventional mechanical alignment (MA) approach: adjusted mechanical (aMA), anatomic (AA), kinematic (KA), restricted kinematic (rKA), and functional (FA) alignment techniques. Among these options, the KA technique is the most extensively studied alternative to mechanical alignment and represents the greatest departure from the conventional approach.

However, the decision to switch to novel (and often more interesting) surgical techniques should be based solely on scientific evidence and not on enthusiasm alone. It is crucial to question the superiority of these new alignment techniques over the traditional MA technique before applying them. Additionally, some authors became concerned about restoring severe pathoanatomies, which may not be compatible with current TKA prostheses and fixation methods, potentially leading to complications and shorter implant survival.

This review aims at answering the following question: do these alternative techniques for implant alignment improve functional outcomes of TKA (primary outcome)? Additional outcomes monitored include knee balance, postoperative alignment, and the rate of complications of TKA.

Methods

Four authors performed a literature search on December 2022 with the electronic database PubMed and Google Scholar. The search parameters used for Pubmed were: (“primary total knee arthroplasty” or “total knee arthroplasty” or “TKA” or “knee arthroplasty” or “primary total knee replacement" or "total knee replacement" or "TKR" or "knee replacement"") and ("alignment" or "knee alignment" or "implant alignment" or "limb alignment" or "joint line alignment" or "positioning" or "implant positioning"); and the search parameters used for Google Scholar database were: ("primary total knee arthroplasty" or "total knee arthroplasty" or "TKA" or "knee arthroplasty" or "primary total knee replacement" or "total knee replacement" or "TKR" or "knee replacement"") and ("alignment"), with words occurring anywhere in the article. Among the studies that were identified, we included retrospective, prospective and randomized clinical trials published over the last 15 years (December 2007 – December 2022) in either English, French or Portuguese, and comparing clinical outcomes between MA-TKA and an alternative technique to position TKA implants. We excluded meta-analysis, systematic reviews, case reports, editorials/opinions, and animal studies.

Three reviewers applied eligibility criteria and selected studies for inclusion in the systematic review; this screening was done independently, and the researchers were blinded to each other's decisions. Disagreements between individual judgments were resolved by a fourth reviewer. Decisions were recorded in EndNote.

Four people independently extracted data, which was synthesized in tables and recorded in an Excel spreadsheet. Data extracted included the year of publication, study design, sample size and alignment options compared, follow-up (years), surgical technique, preoperative patient selection, balancing procedures performed, knee balance, patient-reported outcome measures, postoperative range of motion, postoperative alignment, and the number of complications.

A formal risk of bias assessment was performed independently by four authors (the ones who extracted the data from each study), using the Cochrane risk of bias tool.

Results

We found 10 eligible articles [13-23], whose characteristics are resumed in Table I, Table II and Table III. Figure 1 illustrates the flow diagram of paper selection to answer our question. This PRISMA 2020-compliant flow diagram was created using an online tool [24].

Functional outcomes – Patient-reported outcome measures and range of motion

Anatomic alignment vs Mechanical alignment

We only found one randomized trial to address this question. Yim et al. [14] conducted a comparison between 56 MA TKAs and 61 AA-TKAs, all of which were performed using robotics.

After a minimum follow-up period of 2 years, they observed no significant differences between the two groups in terms of the Hospital for Special Surgery (HSS) and The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, as well as knee flexion. The MA group exhibited scores of 95 (SD 6) and 20 (SD 2), and a knee flexion of 129° (SD 11.5°), while the AA group had scores of 93 (SD 8) and 19 (SD 2), and a knee flexion of 125° (SD 11.5°).

Kinematic alignment vs Mechanical alignment

To address this question, a total of six randomized controlled trials [15-17, 19-21] involving 340 KA TKAs were deemed suitable; these trials resulted in eight reports, as two of them represented follow-up extensions of initial studies [13, 18]. One prospective cohort also met our inclusion criteria [22].

Dossett et al. [15], following a 2-year follow-up, determined that the KA-TKA group outperformed the MA-TKA group in terms of OKS (KA group: mean OKS 40, MA group: mean OKS 33, p = 0.005), WOMAC score (KA group: mean WOMAC 15, MA group: mean WOMAC 26, p = 0.005), and combined KSS (KA group: mean combined KSS 160, MA group: mean combined KSS 137, p = 0.005). Calliess et al. [17] also reported a better functional outcome in the KA group based on the WOMAC score, although not in the combined KSS. Young et al. [21], whose study had the longest follow-up period included in this review, also evaluated OKS, WOMAC, and combined KSS scores in their patient population. They found no statistically significant differences between the MA group (mean OKS 41.7, mean WOMAC 89.1, KSS pain/motion 74.2) and the KA group (mean OKS 41.4, mean WOMAC 86.1, KSS pain/motion 74.6), which was consistent for other patient-reported outcome measures (PROMs) analyzed in the trial (EQ-5D-5L, FJS). The three remaining RCTs [16, 19, 20] likewise observed similar mean scores, including the KOOS.

In their study, McEwen et al. [19] conducted a bilateral simultaneous total knee arthroplasty, allowing them to assess preference. Significantly more participants who favored one knee preferred their KA-TKA (p = 0.03); however, half of the patients had no preference, and the overall numbers were small.

Regarding the range of motion, Dossett et al. [15] found a statistically significant difference of 8.5 degrees in knee flexion (KA group: mean 121, MA group: 113, p = 0.002). However, other RCTs that assessed ROM [16, 18, 19] found similar flexion ranges between groups. Likewise, the RCT comparing anatomic alignment with mechanical alignment [14] found no variations in terms of range of motion.

Knee balance

An RCT [20] revealed that the KA group had a significantly higher proportion of balanced knees at 10° of flexion (defined by an intercompartmental pressure difference of ≤ 15psi) compared to the MA group (KA group: 80% vs MA group: 35%, $p < 0.001$), and also exhibited significantly lower intercompartmental pressure differences at all degrees of flexion assessed. One prospective cohort [22] conducted by the same author yielded similar results; additionally, this paper describes a Coronal Plane Alignment of the knee (CPAK) classification of the knee and concludes that the higher percentage of balanced knees at 10º of flexion verified in the KA group was particularly significant among patients with a knee phenotype equivalent to CPAK types I (KA group: 100% vs MA group: 15%, $p < 0.001$) and IV (KA group: 89% vs MA group: 0%, $p < 0.001$).

Additionally, MacDessi et at. [20] concluded that the MA approach was associated with a greater proportion of TKAs requiring bone recuts to achieve knee balance compared to KA (KA group: 9% vs MA group: 49%, $p < 0.001$). Other studies [13, 19] also reported that the KA group required more ligament releases to produce target laxity values.

Postoperative alignment

All RCTs examining the overall coronal limb alignment (hip-knee-ankle angle) reported similar findings for both the KA/AA and MA groups [14, 15, 19-21]. However, Dossett et al. [15], McEwen et al. [19], and Young et al. [21] observed that in the KA group, the tibial component was tendentially more varus, while the femoral component tended to be more valgus. Additionally, Young et al. [21] discovered that in the KA group, 31% of tibias were in more than 5º varus, which was higher than the percentage observed in the MA group (4%).

Complications

Dossett et al. [15] found no statistically significant difference in the proportion of patients requiring further surgery in either group ($p = 1.00$). Young et al [21] reached similar conclusions, as they observed similar 5-year Kaplan-Meier survivorship free from reoperation/revision (KA group: 92.2%, MA group: 89.7%).

Discussion

In total knee arthroplasty, positioning components to achieve a neutral limb mechanical alignment is a well-established principle. This approach aims to distribute loads evenly and enhance durability [25-29]. In contrast, kinematic alignment (KA) in TKA focuses on replicating the patient's original joint anatomy before arthritis, allowing for better soft tissue balance and potentially improving functional outcomes [8, 13, 30]. Before considering a change in technique, it is necessary to provide clear evidence of functional advantages in KA compared to MA, given the excellent long-term results of the latter. However, there has been ongoing controversy as some studies suggest that KA-TKA may be superior to MA-TKA in terms of enhancing knee motion range and patient satisfaction, while others report no significant difference. Therefore, a systematic review of existing literature is important to establish a more conclusive consensus.

Our systematic review did not demonstrate improved patient-reported outcome scores in KA compared to the MA technique at a 5-year follow-up [21]. At a 2-year follow-up, Dossett et al. reported better functional outcomes with KA-TKA, but it's worth noting that the MA group used manual instrumentation while the KA group utilized patient-specific instrumentation (PSI). Although previous studies found no difference in patient-reported outcomes between PSI and manual instrumentation [31], a systematic review and meta-analysis did identify a small but statistically significant advantage for PSI at the 24-month mark, based on factors like KSS function, KSS knee scores, and WOMAC scores [32]. Hence, it raises questions as to whether the superior PROMs scores observed by Dossett et al. can be attributed solely to kinematic alignment or if the use of PSI in the KA group played a role, unlike in the MA group. Regarding postoperative range of motion, most studies included in our review found no significant differences. Only one trial [12] reported an 8.5-degree difference in knee flexion, but its limitations were discussed earlier.

The comparable functional outcomes observed in kinematic and mechanical alignment do not support the theoretical advantage of restoring the patient's natural alignment. Muertizha et al. [23] devised a nomogram model to predict dissatisfaction one year after total knee arthroplasty (TKA). This model emphasized that the rate of change in the coronal lower limb alignment served as a significant risk factor in predicting patient dissatisfaction. Consequently, the most dissatisfied individuals were those with more severe pathoanatomies, for whom transitioning to a neutral alignment resulted in a substantial change in coronal limb alignment. Considering that some of our trials [16-19, 21] excluded patients with more severe pathoanatomies, it raises the question whether the patients who would benefit the most from kinematic alignment were left out of these studies.

When evaluating the need for intraoperative balancing procedures and proportion of balanced knees, the advantage of kinematic alignment over mechanical alignment is evident and substantial. This outcome was anticipated due to the contrasting surgical technique philosophies. One of the primary goals of kinematic alignment is to restore the patient's physiological soft-tissue balance, thereby reducing the necessity for bone cuts and ligament releases.

Overall, the coronal limb alignment (hip-knee-ankle angle) was similar between KA and MA groups, although the tibial component tended to be slightly more varus in the KA group, while the femoral component tended to be more valgus. The reason may be the different concepts of the two alignment techniques in guiding knee arthroplasty. The impact of these differences on component survival remains uncertain. While there is biomechanical evidence suggesting that varus alignment of the tibial component increases stress at the implant-bone interface [33, 34], clinical evidence on its long-term effects is mixed [29, 35]. The extent of postoperative varus or valgus alignment is likely to be significant [34], but data defining acceptable parameters are currently limited. In the face of this uncertainty, some of the included studies expressed safety concerns and restricted postoperative angles such as HKA angle, lateral distal femoral angle (LDFA), and medial proximal tibial angle (MPTA) within a "safer zone" [19, 20, 22]. The exclusion of patients with more severe pathoanatomies from certain trials [16-19, 21] could also be seen as a reflection of these safety concerns.

The rates of short-term complications and surgical revisions were similar between KA and MA-TKAs in all studies, and the 5-year Kaplan-Meier survivorship free from reoperation/revision was also comparable [21]. Notably, there was no apparent increase in patellofemoral complications in the KA group. The patellofemoral articulation is particularly relevant since there is currently no implant specifically designed for KA. The rotational differences of the femoral component between KA and MA techniques could potentially affect patellofemoral tracking. Whether KA-TKA can lead to patellofemoral joint complications has been a controversial hotspot. Some studies suggest that combined internal rotation of the components in KA-TKA may lead to complications like lateral subluxation or patellar implant failure [36]. Furthermore, a case study [37] indicated increased contact stress of the patellofemoral and tibiofemoral joints, which may increase the risk of prosthesis wear. However, recent research [38, 39] indicates that KA-TKA using a conventional prosthesis does not result in abnormal patellofemoral alignment and can achieve alignment closer to normal. Nevertheless, conclusions regarding complications following KA-TKAs can only be drawn after longer follow-ups than what is currently available.

The risk of bias assessment of the included studies revealed some concerns regarding their internal validity. The primary reason for these concerns was the inability to blind the surgeon and the variability in their experience with different alignment options. Typically, surgeons have greater familiarity with mechanical alignment. Additionally, some studies introduced a confounding variable by utilizing different surgical techniques across groups, including conventional measured resection instruments, patient-specific instrumentation, and computer navigation. Our review exhibited certain methodological shortcomings as well. We limited our search to only two databases, whereas including additional databases such as Scopus and Web of Science could have yielded more relevant studies. Furthermore, we neglected to perform a citation search, which involves using known relevant papers to identify additional related papers.

Conclusion

We found no difference in 5-year functional outcomes in TKAs implanted using the KA compared with the MA technique. Currently, the influence of component alignment variations associated with KA on the longevity of TKA implants and long-term complications remains uncertain. To achieve a more comprehensive understanding of the long-term effects of this alternative approach, it is crucial to conduct further trials that encompass a broader selection of patients and employ extended follow-up periods. Additionally, the creation of implants specifically tailored for KA may be worth exploring. Considering the absence of a definitive functional benefit with kinematic alignment, it is advisable to exercise caution in its utilization until its long-term impact on implant durability is better understood.

Appendix – tables and figures

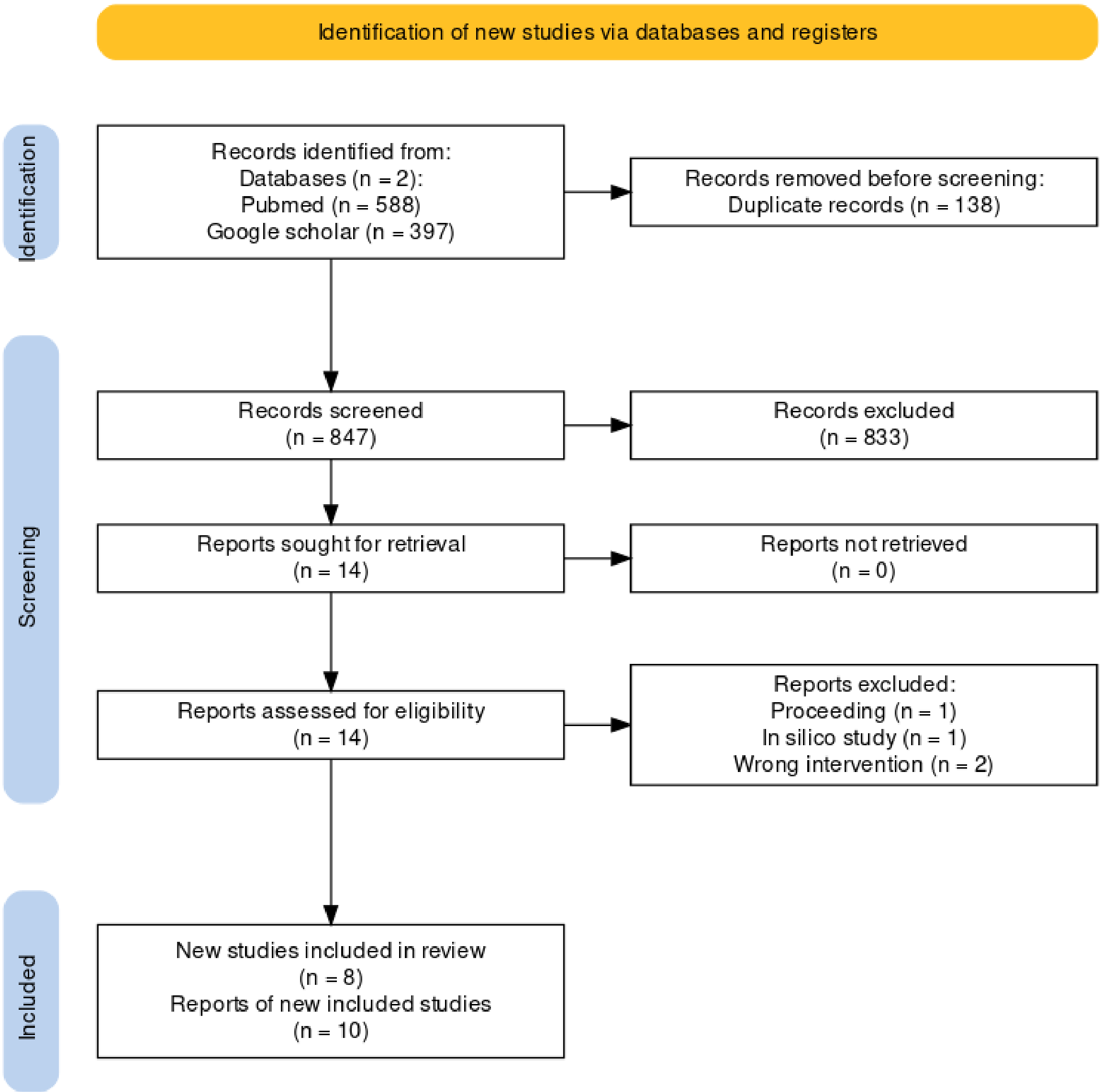

Figure 1 - PRISMA 2020-compliant flow diagram.

Table I - Features and synthesis of findings from relevant studies addressing our question

	Year	Study design	Sample size (knees)	Follow up (years)	Surgical technique / Type of implant	Preoperative patient selection
Yim et al. [14]	2013	RCT – not blinded	MA: 56 AA: 61	2	Both groups: NexGen cruciate-retaining prosthesis (Zimmer Biomet). Patellar resurfacing not performed. Implants fixed with cement. ROBODOC (Integrated Surgical Systems, Davis, California). MA group: Tibial cut and distal femoral cut perpendicular to the mechanical axis. Rotational alignment of the femoral component: parallel to the transepicondylar axis. AA group: Tibial cut: 2° of varus to the mechanical axis of the tibia. Femoral cut: 2° of valgus to the mechanical axis. Rotational alignment of the femoral component: 2° of internal rotation from the transepicondylar axis.	Excluded: - Patients with valgus deformity
Dossett et al. [13, 15]	2012 / 2014	Double blind RCT	MA: 44 KA: 44	½ / 2	MA: conventional measured resection instruments, with 3º external rotation of femoral component KA: PSI (ShapeMatch Technology [Otismed Stryker]) Both groups: cruciate-retaining implant (Vanguard TKA [Biomet]), with patella resurfaced	No
Waterson et al. [16]	2016	Double blind RCT	MA: 35 KA: 36	1	MA: conventional measured resection instruments KA: PSI (ShapeMatch TechnologyTM (Otismed Stryker)) Both groups: cruciate-retaining, cemented, fixed-bearing implant (TriathlonTM; Stryker, Inc), with patella resurfaced	Excluded: - Preoperative varus–valgus deformity >10° - Fixed flexion contracture >20°
Calliess et al. [17]	2016	RCT – not blinded	MA: 100 KA: 100	1	MA: conventional measured resection instruments. Rotation of the femoral component was bony referenced to the transepicondylar line and the Whiteside's line with strict posterior referencing KA: PSI (ShapeMatch Technology TM [Otismed Stryker]) Both groups: cruciate-retaining, cemented, fixed-bearing; implant (TriathlonTM; Stryker, Inc)	Excluded: - Preoperative varus–valgus deformity >10° - Lateral distal femoral angle and/or medial proximal tibial angle outside 86°–94°
McEwen et al. [19]	2019	Double blind RCT	MA: 41 KA: 41	2	Imageless computer navigation system (Precision CAS eNact Knee Navigation System v4.0 software; Stryker Leibinger, Freiburg, Germany). Cruciate-retaining, fixed-bearing implant (Triathlon; Stryker Orthopedics, Mahwah, NJ) with hybrid fixation (cementless femur, cemented tibia). Patellar resurfacing was performed if the lateral patellar facet was not macroscopically normal (KA group: 25; MA group: 23)	Excluded: - Pre-operative valgus deformity

					KA: prescribed postoperative HKA angle limits from 6° varus - 3° valgus	
MacDessi et al. [20]	2020	Double blind RCT	MA 68 KA: 70	1	All TKA (Model Legion, Smith&Nephew) were implanted using computer-assisted navigation (OrthoMap Precision Navigation; Stryker). Posterior stabilized, fully cemented total knee prosthesis, with patellar resurfacing in all cases (Legion; Smith&Nephew, Memphis, Tennessee, USA) KA: restrictive alignment in a safer zone of 4° valgus - 3° varus for LDFA, 3° valgus - 4° varus for MPTA, 5° varus - 4° valgus for HKA. In patients with history of medically treated osteoporosis, insufficiency fractures, >80 years old: safer zone for LDFA and MPTA 3° valgus - 3° varus, HKA to 4° varus - 3° valgus.	No
Young et al. [18, 21]	2017 / 2020	Double blind RCT	MA: 50 KA: 49	2 / 5	MA: computer navigated TKA. Posterior femoral cut made with navigation assistance parallel to the surgical epicondylar axis with Whiteside's line and 3° external rotation relative to the posterior condylar axis used as additional references. KA: PSI (ShapeMatch Technology TM [Otismed Stryker]) Both groups: cruciate-retaining, cemented, fixed-bearing implant (TriathlonTM; Stryker, Inc)–selective patella resurfacing (grade 4 chondral loss on the patella or patellofemoral maltracking)	Excluded: - Preoperative varus–valgus deformity >15° - Fixed flexion contracture >15°
MacDessi et al. [22]	2021	Prospective cohort	MA: 68 KA: 70	NA	Optical navigation (Orthomap Precision Navigation, Stryker, Mahwah, New Jersey, USA) to ensure accurate restoration of target alignments. Posterior-stabilized, fully cemented total knee prosthesis with patellar resurfacing in all cases (Legion, Smith&Nephew, Memphis, Tennessee, USA). KA: prescribed postoperative HKA angle limits from 5° varus to 4° valgus (LDFA/MPTA from 86° to 93°)	No

Table II - Features and synthesis of findings from relevant studies addressing our question (cont.)

	Balancing procedures	Knee balance	PROMs
Yim et al. [14]	Soft tissue balancing, releasing only what was required to achieve balance. Order of release for medial soft tissues: deep MCL, posterior medial capsule, superficial MCL. No lateral releases.	NR	MA group: HSS 94.8 (SD 5.5), WOMAC 20.4 (SD 1.8). AA group: HSS 93.2 (SD 8), WOMAC 19.3 (SD 1.9). No difference intergroup (HSS p = 0.28; WOMAC p = 0.64).
Dossett et al. [13, 15]	MA group: release of the collateral and retinacular ligaments was performed when necessary, at the discretion of the co-surgeons. KA group: collateral or posterior cruciate ligament release was not needed.	NR	MA group: mean OKS 33 (SD 11.1, range 13-48), mean WOMAC 26 (SD 22.6, range from 0 to 73), mean combined KSS 137 (SD 37.9, range 64-200). KA group: mean OKS 40 (SD 10.2, range 15-48), mean WOMAC 15 (SD 20.3, range 0-60, with 0 the best), mean combined KSS 160 (SD 31.9, range 93-200); Difference **Oxford Knee Score (OKS)**: 6.2 points (1.7-10,7) (p = 0.005). Difference **WOMAC score**: −10.7 (−19.8 - −1.5) (p = 0.005). Difference **combined KSS**: 23.3 (8.4 to 38.1) (p = 0.005).
Waterson et al. [16]	NR	NR	Slight improvement in the mean "American Knee Society Score" (at six weeks only) and in the mean physical component of the SF-36 (at six months only) in the KA group, but not statistically significant (p = 0,05 and p = 0.04, respectively). No significant difference in the mean KOOS and EQ-5D scores. No significant difference in functional tests ("time up and go", two-minute walking distance, timed stairs, peak quadricep/hamstring torque).
Calliess et al. [17]	NR	NR	MA group: Mean combined KSS 178 (SD 17), mean WOMAC 26 (SD 11) KA group: Mean combined KSS 190 (SD 18), mean WOMAC 13 (SD 16) p = 0.02 and 0.001 for comparison for KSS and **WOMAC**, respectively
McEwen et al. [19]	More ligament releases were required to produce the target laxity values in the MA group (KA group: 31 vs MA group: 47)	NR	MA group: mean OKS 44.1 (SD 4.1, range 32-48), mean FJS 79.6 (SD 19.4, range 19-100) KOOS - symptoms 89.2 (SD 11.1, range 39-100); pain 91.9 (SD 14.8, range 33-100); daily living 93.5 (SD 9.9, range 53-100); sport 62.3 (SD 28.3, range 0-100); quality of life 85.0 (SD 13.9, range 56-100) KA group: mean OKS 44.4 (SD 4.3, range 30-48), mean FJS 79.9 (SD 23.5, range 0-100) KOOS - symptoms 89.1 (SD 11.3, range 50-100); pain 93.3 (SD 13.0, range 42-100); daily living 93.7 (SD 9.3, range 57-100); sport 61.5 (SD 25.0, range 0-100); quality of life 85.8 (SD 13.9, range 50-100) No significant differences between groups.
MacDessi et al. [20]	ICPD 16-40psi → soft tissue release ICPD >40psi or absolute pressure in one compartment >60 psi→ bony resection Aim: final ICPD ≤ 15 psi;	**At 10º flexion**: MA 32.0; KA 11.7psi p<0.001 **% balanced knees (ICPD≤15) at 10º**: MA 35%; KA 80% p<0.001	MA group: KOOS - symptoms 77 (SD 14.6); pain 85.4 (SD 16.0); daily living 84.5 (SD 16.4); sport 57.4 (SD 29.1); quality of life 71.5 (SD 21.8) FJS-12: 56.8 (SD 26.0) EQ-5D-5L: 82.3 (SD 13.3)

	single compartment pressure ≤ 40 psi Bone recuts to achieve knee balance were more likely to be required in the MA group (49% vs 9%); p<0.001	**At 45º flexion**: MA 25.2; KA 14.8psi p=0.004 **At 90º flexion**: MA 19.1; KA: 11.7psi p<0.002	KA group: KOOS - symptoms 80.5 (SD 16.5); pain 86.7 (SD 16.1); daily living 86.5 (SD 15.2); sport 62.3 (SD 25.4); quality of life 75.1 (SD 22.6) FJS-12: 63.9 (SD 26.6) EQ-5D-5L: 84.1 (SD 15.2) No significant differences between groups.
Young et al. [18, 21]	Ligamentous release was performed if necessary to achieve symmetric ligament balance in both flexion and extension.	NR	MA group: mean FJS 74.4 (SD 23.6) mean OKS 41.7 (SD 6.3) mean KSS Pain/Motion 74.2 (SD 9.0), KSS functional 86.7 (SD 16.8) mean WOMAC score 89.1 (SD 15.3) mean EQ-5D VAS Score 78.4 (SD 17.1) KA group: mean FJS 68.0 (SD 28.8) mean OKS 41.4 (SD 7.2) mean KSS Pain/Motion 74.6 (SD 12.2), KSS functional 81.0 (SD 18.4) mean WOMAC score 86.1 (SD 15.5) mean EQ-5D VAS Score 78.2 (SD 16,5) No significant differences between groups.
MacDessi et al. [22]	ICPD 16-40psi → soft tissue release ICPD >40psi or absolute pressure in one compartment >60 psi→ bone recuts Higher proportion of TKAs requiring bone recuts to achieve knee balance in CPAK types I, II and III when MA was performed compared to KA.	**At 10º flexion** (CPAK type I/IV): MA group: 55.9 / 45.6 psi KA group: 6.5 (p<0.001) / 11.6 psi (p=0.006) **% balanced knees (ICPD≤15) at 10º:** MA group (CPAK I/IV): 15 / 0% KA group (CPAK I/IV): 100 (p<0.001) / 89% (p<0.001) **At 45º flexion** (CPAK type I/IV): MA group: 39.7 / 33.6 psi KA group: 8.7 (p=0.004) / 15.2 psi (p=0.041) **At 90º flexion** (CPAK type I/II): MA group: 28.2 / 18.5 psi KA group: 7.3 (p=0.008) / 12.4 psi (p=0.039)	NR

Table III - Features and synthesis of findings from relevant studies addressing our question (cont.)

	Postoperative range of motion	Postoperative alignment	Complications
Yim et al. [14]	MA group: mean 129° (SD 11.5°) AA group: mean 125° (SD11.5°), p = 0.07	Mean mechanical axis: MA group: −0.71° ± 1.73° AA group: −0.39° ± 2.01°, p=0.76 Coronal alignment of femoral component MA group: 89.5° ± 0.39° AA group: 91.71° ± 1.93°, p= 0.03 Coronal alignment of tibial component: MA group: 90.1° ± 0.37° AA group: 87.48° ± 1.68°, p= 0.04	NR
Dossett et al. [13, 15]	MA group: mean 113° (SD 12,5°, range 80°-130°) KA group: mean 121º (SD 10,4°; range 100°-150°) Difference knee flexion 8,5° (range 3,6°-13,4°) (p=0,002)	Hip Knee Ankle angle: MA group: -0.1° (SD 2.5°, range -8.9° to 4.9°) KA group: 0.1° (SD 2,8°, range -7,7° to 8.5°), p=0.818 **Femoral component alignment relative to femoral mechanical axis:** MA group: 0.8° (SD 2.7°, range -6.3° to 5.8°) KA group: -1.3° (SD 2.0°, range -6.5° to 2.4°), p<0.001 **Tibial component alignment relative to tibial mechanical axis:** MA group: 0.0° (SD 2.1°, range -3.8° to 6.4°) KA group: 2,2° (SD 2.6°, range -4.0° to 8.7°), p<0.001	MA group: 1 **revision** for knee instability + 1 evacuation of hematoma + 1 excision of lateral patella + 1 ORIF patella fracture. KA group: 1 evacuation of hematoma + 2 excisions of lateral patella + 1 reoperation por patellar subluxation There was no statistically significant difference in the proportion of patients requiring further surgery in either group, p = 1,00
Waterson et al. [16]	MA group: Mean 118.4° (SD 9.4°) KA group: Mean 118.5° (SD 12°) Difference: 0.1° (range from −6.1° to 6.2°) (P = 0.98)	Hip Knee Ankle angle: MA group: range 172° to 186° KA group: range 172° to 195° *180° = neutral alignment	MA group: 1 patient with quadriceps rupture KA group: none
Calliess et al. [17]	NR	Hip Knee Ankle angle: MA group: 1° varus (SD 3°) KA group: 1° valgus (SD 3°) LDFA: MA group: 89° (SD 0°) KA group: 88° (SD 1°) MPTA MA group: 89° (SD 0°) KA group: 88° (SD 1°)	MA group: 1 **revision** for knee instability KA group: 2 **revisions** for knee instability
McEwen et al. [19]	MA group: mean 127º (SD 11º; range 105-150) KA group: mean 127º (SD 10º; range 101-154) p = 0.976	HKA angle (at 2 years): MA group: 0.2° varus KA group: 1.0° varus (p=0.97) **Joint line orientation angle** (at 2 years): MA group: 0.8° valgus KA group: 0.9° varus (p=0.002) **Femoral components coronal angle** (intraoperative data): MA group: 0.1° varus KA group: 1.8° valgus (p<0.001) **Tibial components coronal angle** (intraoperative data): MA group: 0.3° varus KA group: 2.5° varus (p<0.001)	MA group: 1 asymptomatic patellar stress fracture KA group: 1 popliteous release for persistent lateral knee pain + 1 two-stage revision for a deep periprosthetic infection) MA + KA: 2 patients with inadequate progression of flexion range in both knees (bilateral manipulation under anesthesia)

MacDessi et al. [20]	NR	HKA: MA group: 0.6° varus (SD 2.3°, range 6° varus - 4° valgus) KA group: 0.2° varus (SD 2.3°, range 5° varus - 5° valgus) No significant difference **LDFA**: MA group: 90.6° (SD 1.5°, range 86°-93°) KA group: 89.2° (SD 1.8°, range 85°-93°) p<0.001 **MPTA** MA group: 90.0° (SD 1.9°, range 85°-94°) KA group: 88,9° (SD 1.8°, range 84°-95°) p=0.003	NR
Young et al. [18, 21]	At 2 years: MA group: Mean 116° (SD 11°, range 90° - 140°) KA group: mean 119° (SD 11°, range 80° - 150°) p = 0.9	Hip Knee Ankle angle MA group: 0.7° varus (SD 2°, range 5° varus - 4° valgus) KA group: 0.4° varus (SD 3°, range 11° varus - 6° valgus). p=0.6 **Femoral component alignment relative to femoral mechanical axis**: MA group: 0.5° valgus (SD 1.6°, range 3° varus - 4° valgus) KA group: 2° valgus (SD 2.5°, range 4° varus - 6° valgus). p=0.002 **Tibial component alignment relative to tibial mechanical axis**: MA group: 0.7° varus (SD 1.8°, range 6° varus - 2° valgus) 4% of tibias were ≥5° varus KA group: 3° varus (SD 3°, range 10° varus - 4° valgus). p<0.001 **31% of tibias were ≥5° varus**	MA group: 1 periprosthetic fracture (due to fall) with subsequent deep infection (two-stage **revision**) + 1 deep infection + 1 recurrent hemarthroses, stiffness and pain + 1 acute patella dislocation (due to fall). One patient (asymptomatic with high functional scores) demonstrated possible radiographic aseptic loosening. KA group: 1 patient with dislocated patella and deep infection, 2 patients stiffness, 1 intermittent pain and locking, 1 late-onset pain and swelling 5-year Kaplan-Meier survivorship free from reoperation/revision: similar KA group: 92.2 (95%CI 80.4 to 97.0) MA group: 89.7 (95%CI 77.0 to 95.6)
MacDessi et al. [22]	NR	NR	NR

+ : varus, - : valgus

References

1. Long, H., et al., *Prevalence Trends of Site-Specific Osteoarthritis From 1990 to 2019: Findings From the Global Burden of Disease Study 2019.* Arthritis Rheumatol, 2022. **74**(7): p. 1172-1183.
2. Adie, S., et al., *Selecting and optimising patients for total knee arthroplasty.* Med J Aust, 2019. **210**(3): p. 135-141.
3. Freeman, M.A., S.A. Swanson, and R.C. Todd, *Total replacement of the knee using the Freeman-Swanson knee prosthesis.* Clin Orthop Relat Res, 1973(94): p. 153-70.
4. Scuderi, G.R., W.N. Scott, and G.H. Tchejeyan, *The Insall legacy in total knee arthroplasty.* Clin Orthop Relat Res, 2001(392): p. 3-14.
5. Patil, S., et al., *How do knee implants perform past the second decade? Nineteen- to 25-year followup of the Press-fit Condylar design TKA.* Clin Orthop Relat Res, 2015. **473**(1): p. 135-40.
6. Price, A.J., et al., *Knee replacement.* Lancet, 2018. **392**(10158): p. 1672-1682.
7. Collins, M., et al., *Joint perception after hip or knee replacement surgery.* Orthop Traumatol Surg Res, 2012. **98**(3): p. 275-80.
8. Nam, D., R.M. Nunley, and R.L. Barrack, *Patient dissatisfaction following total knee replacement: a growing concern?* Bone Joint J, 2014. **96-b**(11 Supple A): p. 96-100.
9. Abdel, M.P., et al., *Effect of Postoperative Mechanical Axis Alignment on Survival and Functional Outcomes of Modern Total Knee Arthroplasties with Cement: A Concise Follow-up at 20 Years.* J Bone Joint Surg Am, 2018. **100**(6): p. 472-478.
10. Kutzner, I., et al., *Knee adduction moment and medial contact force--facts about their correlation during gait.* PLoS One, 2013. **8**(12): p. e81036.
11. Ma CB, L.K., Schrumpf MA, Majumdar S. , *Analysis of three-dimensional in vivo knee kinematics using dynamic magnetic resonance imaging.* Oper Tech Orthop, 2005. **15**: p. 57-63.
12. Howell, S.M., et al., *Results of an initial experience with custom-fit positioning total knee arthroplasty in a series of 48 patients.* Orthopedics, 2008. **31**(9): p. 857-63.
13. Dossett, H.G., et al., *Kinematically versus mechanically aligned total knee arthroplasty.* Orthopedics, 2012. **35**(2): p. e160-9.
14. Yim, J.H., et al., *A comparison of classical and anatomical total knee alignment methods in robotic total knee arthroplasty: classical and anatomical knee alignment methods in TKA.* J Arthroplasty, 2013. **28**(6): p. 932-7.
15. Dossett, H.G., et al., *A randomised controlled trial of kinematically and mechanically aligned total knee replacements: two-year clinical results.* Bone Joint J, 2014. **96-b**(7): p. 907-13.
16. Waterson, H.B., et al., *The early outcome of kinematic versus mechanical alignment in total knee arthroplasty: a prospective randomised control trial.* Bone Joint J, 2016. **98-b**(10): p. 1360-1368.
17. Calliess, T., et al., *PSI kinematic versus non-PSI mechanical alignment in total knee arthroplasty: a prospective, randomized study.* Knee Surg Sports Traumatol Arthrosc, 2017. **25**(6): p. 1743-1748.
18. Young, S.W., et al., *The Chitranjan S. Ranawat Award : No Difference in 2-year Functional Outcomes Using Kinematic versus Mechanical Alignment in TKA: A Randomized Controlled Clinical Trial.* Clin Orthop Relat Res, 2017. **475**(1): p. 9-20.
19. McEwen, P.J., et al., *Computer-Assisted Kinematic and Mechanical Axis Total Knee Arthroplasty: A Prospective Randomized Controlled Trial of Bilateral Simultaneous Surgery.* J Arthroplasty, 2020. **35**(2): p. 443-450.

20. MacDessi, S.J., et al., *Restoring the constitutional alignment with a restrictive kinematic protocol improves quantitative soft-tissue balance in total knee arthroplasty: a randomized controlled trial.* Bone Joint J, 2020. **102-B**(1): p. 117-124.
21. Young, S.W., et al., *No Difference in 5-year Clinical or Radiographic Outcomes Between Kinematic and Mechanical Alignment in TKA: A Randomized Controlled Trial.* Clin Orthop Relat Res, 2020. **478**(6): p. 1271-1279.
22. MacDessi, S.J., et al., *Coronal Plane Alignment of the Knee (CPAK) classification.* Bone Joint J, 2021. **103-B**(2): p. 329-337.
23. Muertizha, M., et al., *Factors contributing to 1-year dissatisfaction after total knee arthroplasty: a nomogram prediction model.* J Orthop Surg Res, 2022. **17**(1): p. 367.
24. Haddaway, N.R., et al., *PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis.* Campbell Systematic Reviews, 2022. **18**(2): p. e1230.
25. Bargren, J.H., J.D. Blaha, and M.A. Freeman, *Alignment in total knee arthroplasty. Correlated biomechanical and clinical observations.* Clin Orthop Relat Res, 1983(173): p. 178-83.
26. Aglietti, P. and R. Buzzi, *Posteriorly stabilised total-condylar knee replacement. Three to eight years' follow-up of 85 knees.* J Bone Joint Surg Br, 1988. **70**(2): p. 211-6.
27. Jeffery, R.S., R.W. Morris, and R.A. Denham, *Coronal alignment after total knee replacement.* J Bone Joint Surg Br, 1991. **73**(5): p. 709-14.
28. Ritter, M.A., et al., *Postoperative alignment of total knee replacement. Its effect on survival.* Clin Orthop Relat Res, 1994(299): p. 153-6.
29. Fang, D.M., M.A. Ritter, and K.E. Davis, *Coronal alignment in total knee arthroplasty: just how important is it?* J Arthroplasty, 2009. **24**(6 Suppl): p. 39-43.
30. Howell, S.M., et al., *Accurate alignment and high function after kinematically aligned TKA performed with generic instruments.* Knee Surg Sports Traumatol Arthrosc, 2013. **21**(10): p. 2271-80.
31. Nam, D., et al., *The Mark Coventry Award: Custom Cutting Guides Do Not Improve Total Knee Arthroplasty Clinical Outcomes at 2 Years Followup.* Clin Orthop Relat Res, 2016. **474**(1): p. 40-6.
32. Rudran, B., et al., *Functional outcomes in patient specific instrumentation vs. conventional instrumentation for total knee arthroplasty; a systematic review and meta-analysis of prospective studies.* BMC Musculoskelet Disord, 2022. **23**(1): p. 702.
33. Green, G.V., et al., *The effects of varus tibial alignment on proximal tibial surface strain in total knee arthroplasty: The posteromedial hot spot.* J Arthroplasty, 2002. **17**(8): p. 1033-9.
34. Halder, A., et al., *Influence of limb alignment on mediolateral loading in total knee replacement: in vivo measurements in five patients.* J Bone Joint Surg Am, 2012. **94**(11): p. 1023-9.
35. Parratte, S., et al., *Effect of postoperative mechanical axis alignment on the fifteen-year survival of modern, cemented total knee replacements.* J Bone Joint Surg Am, 2010. **92**(12): p. 2143-9.
36. Berger, R.A., et al., *Malrotation causing patellofemoral complications after total knee arthroplasty.* Clin Orthop Relat Res, 1998(356): p. 144-53.
37. Ishikawa, M., et al., *Kinematic alignment produces near-normal knee motion but increases contact stress after total knee arthroplasty: A case study on a single implant design.* Knee, 2015. **22**(3): p. 206-12.
38. Lozano, R., et al., *Kinematic alignment more closely restores the groove location and the sulcus angle of the native trochlea than mechanical alignment: implications for prosthetic design.* Knee Surg Sports Traumatol Arthrosc, 2019. **27**(5): p. 1504-1513.

39. Keshmiri, A., et al., *Kinematic alignment in total knee arthroplasty leads to a better restoration of patellar kinematics compared to mechanic alignment.* Knee Surg Sports Traumatol Arthrosc, 2019. **27**(5): p. 1529-1534.

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